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REACTIONS FOLLOWING THE USE OF DIPHTHERIA TOXOID

ANALYSIS OF THE REACTIONS AND OF GUIDES TO THEIR OCCURRENCE

CHARLES R. HAYMAN, M.D.

NEW YORK

Undiluted toxoid, plain or fluid, (in contradistinction to alum-precipitated toxoid) is now in general use as an active immunizing agent against diphtheria. Its effectiveness is well established. However, reactions to the injections do occur. Presumably, both the effectiveness and the likelihood of reaction increase with the dose. Therefore, one should try to strike a balance, giving that dose which is just not large enough to produce reaction. To help in finding this there are two suggested guides: (1) the age of the subject and (2) the subject's sensitivity to various cutaneous tests performed previous to injection.

The amount of caution that one must exercise in giving injections of toxoid depends on the expected frequency and severity of reaction. However, there is so much variation in the findings [1] that one cannot obtain from the literature a clear idea as to the extent of reaction.

From the Willard Parker Hospital.

1. (*a*) Beckman, H.: Review of Antitoxin and Toxoid in Diphtheria Immunization, Arch. Pediat. **50**:211 (March) 1933. (*b*) Burke, F.: Administrative Control of Diphtheria Toxoid Campaign in Toronto, Canad. Pub. Health J. **21**:209 (May) 1930. (*c*) Chesney, G.: Formol Toxoid and the Schick Level, M. Officer **54**:186 (Nov. 2) 1935. (*d*) Keller, A., and Harris, S.: Use of Diphtheria Toxoid in the Immunization of Medical Students and Nurses, J. A. M. A. **102**:2163 (June 30) 1934. (*e*) McGinnes, G.; Stebbins, E., and Hart, C.: Experiments with Alum Precipitated Toxoid in Virginia and Observations on Reactions Following Its Use, Am. J. Pub. Health **24**:1141 (Nov.) 1934. (*f*) Mitman, M.: Pseudo-Schick Reaction and Intradermal Test of Moloney, J. Hyg. **35**:512 (Dec.) 1935. (*g*) Moloney, P.; Fraser, D., and Fraser, C.: Immunization contre la diphtérie au moyen de l'anatoxine, Ann. Inst. Pasteur **43**:124 (Jan.) 1929. (*h*) O'Brien, R., and Parish, H.: Immunization with Potent Unconcentrated Diphtheria Toxoid, Lancet **2**:176 (July 23) 1932. (*i*) Swyer, R.: Diphtheria Formol Toxoid and the Moloney Test, ibid. **2**:22 (July 6) 1935; (*j*) Toxoid-Antitoxin Floccules, Alum Toxoid, and Formol Toxoid in Immunization Against Diphtheria, London County Council, report 3013, London, P. S. King & Son, Ltd., 1932, vol. 4, pt. 3, p. 57. (*k*) Underwood, E.: Potent Formol Toxoid as a Diphtheria Prophylactic and Interpretation of the Moloney Test, Lancet **1**:678 (March 31) 1934; (*l*) Diphtheria Toxoid-Reaction (Moloney) Test: Its Application and Significance, J. Hyg. **35**:449 (Dec.) 1935.

Although many investigators have used different doses of toxoid, varying from 0.1 to 1 cc., there has been no report of the effect on reaction of controlled variation in dose.

An increase in the frequency and severity of reaction with increase in age has been noted by Ramon,[2] Burke,[1b] Chesney [1c] and Swyer.[1j]

The use of the Schick control test as a forecaster of reaction has been reported on favorably by O'Brien and others,[3] Mitman,[1f] Roubinovitch and others,[4] and Zoeller.[5] The diluted toxoid test, often referred to as the Moloney test, is done in the same manner as the Schick control test, the material being plain toxoid diluted with a solution of sodium chloride. Favorable reports on the use of this test in forecasting reaction have been made by Burke,[1b] Keller and Harris,[1d] McKinnon and Ross,[6] Moloney and others,[1g] O'Brien and Parish,[1h] Swyer [1i] and Zoeller.[5b] However, when both tests were done on the same subjects Underwood [1l] found the Schick control test worthless as compared with the diluted toxoid test, whereas Mitman [1f] found them equally good. The use of the Schick test in this connection has not been described.

It is the purpose of the present paper, therefore, to answer the following questions regarding prophylactic injections of toxoid:

1. Are reactions to toxoid frequent and severe enough to warrant caution in its use?

2. Is the age of the subject a guide in foretelling the occurrence of reaction?

3. How efficient are the cutaneous tests (Schick control, diluted toxoid, Schick) in forecasting reaction?

4. Is dosage an important factor in controlling the occurrence of reaction?

5. What procedure should be followed in immunizing, so as to avoid reaction and yet give the most effective doses?

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2. Ramon, cited by Beckman.[1a]

3. O'Brien, R.; Gunn, W., and Dudley, S.: Skin Tests in Tuberculosis and Exanthemata, Tr. M. Soc. London **56**:68, 1933.

4. Roubinovitch, J.; Loiseau, G., and Lafaille, A.: Immunization antidiphtérique chez l'enfant avec l'anatoxine diphtérique, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:782 (May 23) 1924.

5. Zoeller, C.: (*a*) La vaccination par l'anatoxine diphtérique chez l'adulte, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:644 (May 9) 1924; (*b*) L'anatoxine-réaction, ou protéino-réaction révélatrice de l'allergie diphtérique, ibid. **48**:1032 (July 4) 1924.

6. McKinnon N., and Ross, M.: Diphtheria Toxoid Reaction Test in Thirty Thousand Children, Canad. Pub. Health J. **24**:496 (Oct.) 1933.

METHODS

Three cutaneous tests (Schick, Schick control and diluted toxoid) were made simultaneously in 289 persons. The results were read on each of the following seven days. Each person was then given an initial injection of undiluted plain toxoid, regardless of the readings. At this time 269 of the subjects were convalescing from various contagious and infectious diseases; the remainder were healthy diphtheria carriers and healthy hospital employees. A second injection was given to 101 of the original group approximately one week after the first injection. The subjects were observed on the first and the second day after each injection, and signs and symptoms of reaction were noted.

All cutaneous tests were done with 0.1 cc. of solution. The diluted toxoid test was done with a 1:20 dilution of the toxoid later used for injection. Except for the diluted toxoid, all the materials were those regularly used at the Willard Parker Hospital, as prepared by the laboratories of the New York city board of health.

The three tests were tabulated separately. The Schick test was considered positive if on any day an area of erythema appeared larger than that of the Schick control test. The Schick control and the diluted toxoid test were considered positive if erythema appeared on any day. (The test readings will be discussed in a paper to be published.) For all three tests, the method of grading was that of Underwood:[11] 1 plus, area of definite redness, not due to trauma, less than 1 cm. in diameter; 2 plus, area of definite redness more than 1 cm. in diameter with no or slight induration; 3 plus, area of definite redness more than 1 cm. in diameter with definite induration.

The signs and symptoms following each injection of undiluted toxoid were then analyzed, and the degree of reaction was determined. The method was similar to that previously used by McGinnes.[1e] Separate tabulations were made for local and for general reactions. Thus each sign and symptom of a local nature noted after a particular injection was given a value of from 1 to 4 plus, as designated in table 1. These values were then added, and the sum was divided by 3. The resulting figure indicated the grade of local reaction present, according to the following scale: 1 plus, mild; 2 plus, moderate; 3 plus, severe.

For example, suppose a person shows the following signs and symptoms of general nature: a temperature of 100 F., moderate nausea and severe headache. The values are, respectively, 1, 2 and 3 plus. The sum is 6 plus; dividing by 3 gives 2 plus. Thus the patient has a moderate general reaction.

The presence of certain signs and symptoms was considered sufficient evidence of reaction, without recourse to the formula just cited. Thus a person was considered to have a mild general reaction if he showed only a temperature of 101 F., a moderate general reaction if he vomited or showed a rash, and a severe general reaction if he had chills or fainted. Similarly, severe redness was considered sufficient evidence of a moderate local reaction; the presence of a local rash was evidence of a severe local reaction.

RESULTS

Frequency of Signs and Symptoms of Reaction to Injection of Undiluted Toxoid.—Since it was often difficult to get those under 15 years of age to answer questions, no statement can be made about their symptoms. In the group above 15 years, the most frequent symptom was headache. The most frequent sign of general reaction

was rise of temperature to 100 F. in the group under 15 and to 101 F. in the group above 15. The most frequent sign of local reaction in both age groups was tenderness.

There was an increase in almost all signs of reaction with increase in age (table 1).

Frequency and Severity of General and Local Reactions.—In all, there were 14.9 per cent general reactions, of which 47 per cent were mild, 28 per cent moderate and 25 per cent severe. There were 9.7 per

TABLE 1.—*Signs and Symptoms of General and Local Reaction to Injection of Undiluted Toxoid in Order of Percentage Frequency*

		Percentage Frequency of Signs and Symptoms		
General reaction	Values (+)*	Age Less Than 15 Years (270 Injections)	Age 15 or More Years (120 Injections)	Total (390 Injections)
Symptoms				
Headache	1, 2, 3†	N‡	10.0	...
Malaise	1, 2, 3	N	9.0	...
Nausea	1, 2, 3	N	9.0	...
Aches and pains	1, 2, 3	N	8.3	...
Dizziness	1, 2, 3	N	5.8	...
Weakness	1, 2, 3	N	3.3	...
Numbness	1, 2, 3	N	2.5	...
Insomnia	1, 2, 3	N	0.8	...
Cramps	1, 2, 3	N	1.6	...
Signs				
Temperature 100 F.	1	8.1	10.0	8.2
Temperature 101 F.	2	5.2	10.8	6.9
Temperature 102 F.	3	1.5	5.8	3.0
Temperature 103 F.	4	0.8	2.5	1.3
Temperature 104 F.	4	0.0	0.8	0.3
Vomiting	4	0.8	3.3	1.5
Chills	4	0.0	3.3	1.1
Fainting	4	0.0	0.8	0.3
Rash	4	0.8	0.0	0.5
Local reaction				
Signs				
Tenderness	1, 2, 3†	14.4	30.0	19.2
Redness	1, 2, 3	10.8	20.0	13.6
Hardness	1, 2, 3	4.8	16.7	8.4
Adenitis	1, 2, 3	0.0	1.7	0.5
Rash, local	3	0.4	0.0	0.3

* Arbitrary values assigned for determination of the presence and the degree of reaction, as described in the section on methods.
† 1+, mild headache; 2+, moderate; 3+, severe.
‡ N, no information on symptoms was obtainable.

cent local reactions, of which 55 per cent were mild, 21 per cent moderate and 24 per cent severe.

The reactions were analyzed with respect to variation in three factors: age of the subject, dose of undiluted toxoid and sensitivity to the cutaneous tests. Thus there were the following groups: those under and those above 15 years of age; those receiving a dose of 0.5 cc. and those receiving a dose of 1 cc. of undiluted toxoid; those with negative and those with positive cutaneous tests (Schick, Schick control and diluted toxoid).

In each of the groups just cited general reactions were more frequent than local reactions. Both types of reaction, however, were affected alike by the variation in each of the three factors considered (table 2).

Effect of Age on Frequency of Reaction.—The age distribution was as follows: The 204 persons below 15 years of age (from 6 weeks to 14 years) received an initial injection of undiluted toxoid, and 66 of these received an additional injection. The 85 persons above 15 years

TABLE 2.—*Frequency of General and Local Reactions to Injection of Undiluted Toxoid as Affected by Variation in Age, Dose and Cutaneous Sensitivity* *

	General Reactions		Local Reactions	
	Number	Percentage	Number	Percentage
Total	58/390†	14.9	38/390	9.7
Age				
Under 15	25/270	9.2	18/270	6.7
Over 15	33/120	27.5	20/120	16.7
Dose of undiluted toxoid				
0.5 cc.	28/ 85	32.9	17/ 85	20.0
1 cc.	30/305	9.8	21/305	6.9
Cutaneous sensitivity				
Diluted toxoid				
Negative	16/243	6.6	6/243	2.4
Positive	42/147	28.6	32/147	21.8
Schick control				
Negative	48/360	13.3	26/360	7.2
Positive	10/ 30	33.3	12/ 30	40.0
Schick				
Negative	34/170	20.0	16/170	9.4
Positive	24/220	10.9	22/220	10.0

* Actual and percentage frequency for all injections.
† In this table and in tables 3 and 5, the numerator of a fraction represents reactions and the denominator injections of toxoid.

TABLE 3.—*Effect of Age on Actual and Percentage Frequency of General Reactions to Toxoid in Groups of the Same Cutaneous Sensitivity Who Received Equal Doses of Undiluted Toxoid*

		Diluted Toxoid		Schick Control		Schick	
Dose	Sensitivity to Cutaneous Test	Under 15 Yr.	Over 15 Yr.	Under 15 Yr.	Over 15 Yr.	Under 15 Yr.	Over 15 Yr.
0.5 cc.	Neg.	10.0%	6.6%	29.6%	27.3%	17.7%	37.5%
		1/10	1/15	7/27	12/44	3/17	9/24
	Pos.	30.0%	50.0%	0%	81.8%	30.8%	38.7%
		6/20	20/40	0/3	9/11	4/13	12/31
1 cc.	Neg.	4.7%	12.8%	8.0%	17.2%	12.4%	31.3%
		8/171	6/47	18/225	11/64	12/97	10/32
	Pos.	14.5%	33.3%	0%	100%	4.2%	6.1%
		10/69	6/18	0/15	1/1	6/143	2/33

(15 to 74 years) received an initial injection, and 35 of these received an additional injection.

General and local reactions occurred three times as often in the older group (table 2). This might have occurred because those in the older group had received the larger dose of undiluted toxoid and had had positive cutaneous tests. To eliminate the influence of the size of the dose and cutaneous sensitivity and to show the effect of variation in age alone, a second analysis was made. Two groups were

compared in which the subjects had received the same dose (0.5 or 1 cc.) and had reacted alike to the cutaneous tests (positively or negatively). The only difference in these two groups was that of age. As in the first analysis, it was found that a larger percentage of reactions occurred in those over 15 years (table 3). This analysis was made only for general reactions, since, as has been shown, local reactions were similarly affected by variations in age, dose and cutaneous sensitivity.

Effect of Cutaneous Sensitivity on Reactions.—General and local reactions to the injection of undiluted toxoid occurred much more frequently in those with positive Schick control and diluted toxoid tests. Those with positive Schick tests, however, had fewer general reactions and the same number of local reactions (table 2).

In the second analysis a comparison was made between groups of the same age who received the same dose of undiluted toxoid. The only difference was that of cutaneous sensitivity. The results were as follows: 1. Among those with positive diluted toxoid tests there were more frequent general reactions in all groups. 2. Among those with positive Schick control tests there were more frequent general reactions only in the group more than 15 years of age. 3. Among those with positive Schick tests there were more frequent general reactions in the group receiving the smaller dose and less frequent general reactions in the group receiving the larger dose (table 4).

TABLE 4.—*Effect of Cutaneous Sensitivity on Percentage Frequency of General Reactions to Toxoid in Groups of the Same Age Who Received Equal Doses of Undiluted Toxoid*

		Percentage of Frequency Reactions					
		Diluted Toxoid		Schick Control		Schick	
Age	Dose	Negative	Positive	Negative	Positive	Negative	Positive
Under 15 yr.	0.5 cc.	10.0	30.0	29.6	0	17.7	30.8
	1 cc.	4.7	14.5	8.0	0	12.4	4.2
Over 15 yr.	0.5 cc.	6.6	50.0	27.3	81.8	37.5	38.7
	1 cc.	12.8	33.3	17.2	100.0	31.3	6.1

The actual frequency of reactions and injections may be found in table 3 under the corresponding percentages.

Effect of Increasing Sensitivity to the Cutaneous Tests: The increased frequency of reaction with increase in the degree of cutaneous sensitivity to the diluted toxoid and to the Schick control test is indicated by the example given in table 5.

Effect of Dose on Frequency of Reaction.—For the purpose of comparison, the doses of undiluted toxoid were divided into two groups: 0.5 cc., 85 injections; 1 cc., 305 injections. The 0.5 cc. group included 8 injections of 0.1 cc. and 9 injections of 0.25 cc. The 1 cc. group

included 4 injections of 2 cc. The dose was selected before injection according to age and cutaneous sensitivity. Small doses were given to older subjects who had positive Schick control and diluted toxoid tests, in order that severe reactions might be avoided. Large doses were given to the younger subjects who had negative tests, in order to bring out reactions.

General and local reactions were three times as frequent in those who received the 0.5 cc. dose as in those who received the 1 cc. dose (table 2). When groups of similar age and cutaneous sensitivity were

TABLE 5.—*Effect of Increasing Cutaneous Sensitivity on Actual and Percentage Frequency of General Reactions to Toxoid in Group Aged 15 or More Years; Dose of Undiluted Toxoid, 0.5 cc.*

Sensitivity to Cutaneous Test	Reaction to Toxoid			
	Diluted Toxoid		Schick Control	
	Number	Percentage	Number	Percentage
Negative	1/15	6.7	12/44	27.3
+1	0/ 5	0	4/6	66.7
+2	6/12	50.0	3/3	100.0
+3	14/23	60.9	2/2	100.0

TABLE 6.—*Effect of Undiluted Toxoid on Percentage Frequency of General Reactions in Groups of the Same Age, and of the Same Cutaneous Sensitivity*

Age	Sensitivity to Cutaneous Test	Percentage Frequency of Reactions					
		Diluted Toxoid		Schick Control		Schick	
		0.5 Cc.	1 Cc.	0.5 Cc.	1 Cc.	0.5 Cc.	1 Cc.
Under 15 yr.	Neg.	10.0	4.7	29.6	8.0	17.7	12.4
	Pos.	30.0	14.5	0	0	30.8	4.2
Over 15 yr.	Neg.	6.6	12.8	27.3	17.2	37.5	31.3
	Pos.	50.0	33.3	81.8	100.0	38.7	6.1

The actual frequency of reactions and injections may be found in table 3 under the corresponding percentages.

compared, the same relation held in the majority of instances: Those who received the smaller dose experienced a larger number of general reactions (table 6).

The findings up to this point were based on the combined figures for first and second injections. When the reactions to first and second injections were compared in the same persons, the findings were as follows: Of those receiving a second dose of undiluted toxoid equal to the first, 3 of 63 subjects, or 4.8 per cent, had greater general and local reactions to the second injection. Of those receiving a second dose double the amount of the first, 6 of 38, or 15.8 per cent, had greater second general reactions, and 7 of 38, or 18.4 per cent, had greater second local reactions.

COMMENT

Frequency and Severity of Reaction.—There are three variable factors inherent in this problem: the dose of material injected, the age of the subject and the standard for determining the presence and degree of reaction. If these factors remained constant in each experiment, the findings of different observers could be compared easily. That this is not the case is shown by the following examples noted in the literature:

1. The initial dose of undiluted toxoid used by Chesney,[1c] Mitman [1f] and Swyer [1j] was 0.1 cc. Moloney and others,[1g] Roubinovitch and others [4] and Zoeller [5b] used 0.5 cc.; Burke,[1b] McGinnes and others [1e] and McKinnon and Ross [6] used 1 cc.

2. Burke,[1b] Chesney,[1c] McKinnon and Ross,[6] Roubinovitch and others [4] and Underwood [11] worked with children. Keller and Harris,[1d] Mitman [1f] and Zoeller [5] worked with adults.

3. Some authors have reported the occurrence of reactions without stating the symptoms and signs of which they were comprised (Chesney,[1c] Keller and Harris,[1d] Moloney and others [1g] and O'Brien and Parish [1h]). Of the others who set up definite standards for the presence and degree of reaction, each used a different combination of symptoms and signs (McGinnes and others,[1e] Mitman,[1f] Roubinovitch and others [4] and Swyer [7]).

Therefore, I have not attempted to present a comparison of my results with those of the previous workers as to the frequency and severity of reaction.

Effect of Age on Frequency and Severity of Reaction.—The positive correlation that I have found between age and frequency of reaction has been reported previously by Ramon,[2] Burke,[1b] Chesney [1c] and Swyer.[1j]

It should be noted that dividing the subjects into those receiving the same dose and having the same skin sensitivity (table 3) has produced some groups too small to be used for statistical analysis. Thus the finding of more frequent reactions in the younger group who had negative cutaneous tests and who received the 0.5 cc. dose (table 3) may be due to the operation of chance in a small sample.

I have not included in my findings the incidence of reaction in subjects under 5 years, since I did not wish to complicate the presentation by introducing more than the two age groups—that below and that above 15 years. It is worth mentioning, however, that there were 7 reactions to the 71 injections of the subjects under 5 years. Two of the 7 were severe. Because of this finding I am inclined to doubt the conclusion of Burke [1b] that among children under 5 years there are

7. Swyer (footnote 1 *i* and *j*).

not enough reactors to injected toxoid to warrant the use of the preliminary diluted toxoid test.

Cutaneous Sensitivity and Reactions.—Schick Test: Immunization of children from 4 to 8 years of age without a preliminary Schick test has often been practiced. If the frequency of reaction to immunization is related to the positivity or negativity of the Schick test, the practice is unwise. According to Burke,[1b] the sensitivity to the Schick test (presumably) indicated no difference in the reactions to immunization. Underwood,[8] however, noted that those with markedly positive Schick tests reacted more strongly to toxoid.

My figures for local reaction showed a negligible difference between subjects with negative and those with positive Schick tests. General reactions to immunization were definitely more frequent in those with negative Schick tests. When these general reactions, however, were analyzed in groups of the same age, who received the same dose of undiluted toxoid, the relation of sensitivity to the test to frequency of general reaction was seen to vary with the dose. From my study, therefore, I am unable to infer a correlation between the sensitivity to the Schick test and the occurrence of reaction to immunization.

Schick Control Test: Underwood,[11] using the test on children, found that it was valueless as a forecaster of reaction. Mitman,[1f] working with adults, found it to be just as good as the diluted toxoid test. My finding that the test was effective only in the group above 15 years indicates that the difference in their results is due to the difference in age of their subjects.

Diluted Toxoid Test: The dose used by different workers in the Schick control test and the Schick test has been fairly constant, but the dose of diluted toxoid has varied greatly. Thus:

Dose (Cc.)	Dilution	Authors
0.1	1:100	Marchand [9]
0.2	1:100	Bozzi,[10] Underwood,[1k] Zoeller [5b]
0.2	1:40	Mitman [1f]
0.1	1:20	Moloney and others [1g]
0.1	1:10	Keller and Harris [1d]
0.2	1:10	Swyer [11]

Because of this variation, the actual relation of the results of test to the frequency of reaction to immunization found by different workers cannot be compared. In general, my findings agree with those of the previous authors, who reported that the test was a good index of the occurrence of reaction to immunization at all ages.

8. Underwood, E.: Immunization Against Diphtheria by Means of a Single Dose of Alum Precipitated Toxoid (A. P. T.), Lancet **1**:138 (Jan. 9) 1935.

9. Marchand, J.: L'anatoxiréaction de Zoeller dans la diphtérie, Thesis, Paris, no. 103, 1925.

10. Bozzi, E.: Può l'anatossireazione di Zoeller avere valore diagnostico-pratico nella difterite? Riv. di clin. pediat. **33**:769 (July) 1935.

Dose of Undiluted Toxoid and Reactions.—I found that those who received the smaller dose experienced more frequent reactions than those who received the larger dose. This paradox is explained by the fact that the smaller dose was given to those of older age and greater cutaneous sensitivity.

As an example, consider those with positive reactions to the diluted toxoid test in the age group below 15 years (table 6). The average age of the 20 subjects who received an injection of 0.5 cc. of undiluted toxoid was 10.5 years, as against 8 years for the 69 who received an injection of 1 cc. Similarly, the average age of the 6 reactors to 0.5 cc. was 12 years, as against 7.6 years for the 10 reactors to 1 cc.

Considering the degree of sensitivity to the diluted toxoid test (mild, 1 plus; moderate, 2 plus; severe, 3 plus), the average sensitivity of those who received 0.5 cc. was 2.3 plus, as against 1.5 plus for those receiving 1 cc. For the reactors the comparison was 2.3 to 2 plus.

In the group with negative sensitivity to the diluted toxoid test, a stronger test would, I believe, similarly bring out more positive reactions in those who received the smaller dose.

That dosage is of little importance as compared to age and cutaneous sensitivity is further illustrated by the fact that decrease in dose alone did not suffice to avoid reaction. Thus of 8 persons given the minimal dose of 0.1 cc. of undiluted toxoid (because they were adults who showed marked sensitivity to the diluted toxoid test), 5 experienced severe general or local reaction. This is in direct contrast to the statement of Beckman:[18a] "Experience has shown that unduly severe reactions in adults may be avoided if the regular doses are preceded by two preliminary doses of 0.1 and 0.25 cc. of the undiluted toxoid. . . ."

The true effect of variation in dose was seen when the effects of initial and subsequent injections in the same person were compared. There was a definite increase in the degree of reaction to the second injection when the second dose was double the first. With a second dose equal to the first, the increase in degree was not significant.

The New York city board of health, in its 1937 bulletin on immunization, advocated giving an initial dose of 0.25 cc. of undiluted toxoid to those over 6 years, to be followed in two weeks, if no reaction has occurred, with a second injection of 1 cc. From my findings it would appear that this method is not the safest, since a definite number of reactions may be expected to result from the second injection.

SUGGESTED PROCEDURE OF IMMUNIZATION

I wish to suggest a scheme for immunization which takes into account the findings of the present study on age, dosage and cutaneous sensitivity.

A. If the subject is 15 years of age or older:

1. Perform preliminary cutaneous tests, using
   (*a*) Schick and Schick control test
   (*b*) or Schick and diluted toxoid (1:20) tests
   (*c*) or all three.
2. If the Schick test is positive, give the first injection as follows:
   (*a*) If the Schick control test, the diluted toxoid test or both are negative, inject 0.5 cc. of undiluted toxoid.
   (*b*) If the highest reading is 1 plus, inject 0.25 cc. of undiluted toxoid.
   (*c*) If the highest reading is 2 plus, inject 0.1 cc. of undiluted toxoid.
   (*d*) If the highest reading is 3 plus, inject diluted toxoid or another material such as toxoid-antitoxin floccules or do not immunize.
3. For subsequent injection:
   (*a*) If no reaction has occurred, give the same or, at most, a double dose.
   (*b*) If a reaction has occurred, give the same or a decreased dose.

B. If the subject is under 15 years of age:

1. Do the preliminary cutaneous tests, using
   (*a*) Schick test alone
   (*b*) or Schick and diluted toxoid tests.
2. If the Schick test is positive, give the first injection as follows:
   (*a*) If the diluted toxoid test was omitted, inject 0.1 cc. of undiluted toxoid.
   (*b*) If the diluted toxoid test reading is 1 plus, inject 1 cc. of undiluted toxoid.
   (*c*) If the diluted toxoid test reading is 2 plus, inject 0.5 cc. of undiluted toxoid.
   (*d*) If the diluted toxoid test reading is 3 plus, inject 0.25 cc. of undiluted toxoid.
3. For subsequent injection, proceed as in *A*.

SUMMARY

Two hundred and eighty-nine persons were given the Schick, Schick control and diluted toxoid tests. Each was then given an initial injec-

tion of undiluted plain toxoid. One hundred and one of these were each given a second injection.

There were 14.9 per cent general and 9.7 per cent local reactions; 25 per cent of these were severe. General reactions were more frequent than local when analyzed in respect to variations of age, sensitivity to the cutaneous tests and size of the dose of undiluted toxoid. Both types of reaction were affected alike by these variations.

There was an increase in reactions with increase in age.

The sensitivity to the Schick test was not definitely related to the occurrence of reaction to the undiluted toxoid. The positive Schick control and diluted toxoid tests showed a fair correlation with the occurrence of reaction to the undiluted toxoid. The more positive the cutaneous test, the higher was the correlation. The positive diluted toxoid test was related to reaction to the undiluted toxoid in both age groups—those under and those above 15 years; the positive Schick control test was so related only in the group above 15 years.

There were 85 injections of 0.5 cc. or less and 305 injections of 1 cc. or more of undiluted toxoid. Those receiving the smaller doses experienced more reactions than those who received the larger doses. The former were older and were more sensitive to the diluted toxoid and to the Schick control test. Severe reactions occurred in the adults who were sensitive to the diluted toxoid test, even though they were given the minimal dose of undiluted toxoid. There was a definite increase in the degree of reaction experienced by the same person when the dose of the second injection was double that of the first; there was no definite increase when the dose remained the same.

A method of procedure for immunization has been described, the purpose of which is to enable one to avoid reaction and yet to give the most effective doses.

CONCLUSIONS

1. Reactions to the injection of undiluted plain toxoid are frequent and severe enough to warrant caution.

2. The age of the subject is a good guide in foretelling reaction.

3. The diluted toxoid test is of value in forecasting reaction in those younger than 15 years; the Schick control test is not. Both are of value in those older than 15 years.

4. Reactions are less influenced by change in dose of undiluted toxoid than by variation in age and cutaneous sensitivity.

5. Lack of reaction to an initial injection does not warrant giving a much stronger second injection.

Medical Centre Building, White Plains, N. Y.

EFFECT OF VITAMIN B_1 ON THE IRON RETENTION OF A NORMAL INFANT

FREDERIC W. SCHLUTZ, M.D.

HELEN OLDHAM, M.S.
AND
MINERVA MORSE, PH.D.
CHICAGO

In previous studies [1] in this laboratory it was observed that the retention of iron by the infant decreased noticeably when the vitamin B_1 content of the diet was increased by supplements of wheat germ. The object of the work to be reported here was to determine whether or not the lowered retention of iron was due to a specific effect of the vitamin. The iron retention and hemoglobin formation found for a normal infant during periods in which the diet was supplemented with a solution of crystalline vitamin B_1 have been compared with those found in control periods during which no vitamin B_1 supplement was given. This comparison has been made at three levels of intake of iron in order to observe both the effect of the vitamin at different levels of iron intake and the effect of the different levels of intake on the retention of iron.

EXPERIMENTAL PROCEDURE

The subject of this experiment was an infant who had been examined routinely in the clinic since birth. The history showed that the mother had a normal pregnancy and a normal spontaneous delivery. The child weighed 4,765 Gm. at birth and had gained normally since that time. He was breast fed for the first three months, after which he received food prepared by formula, consisting of evaporated milk and corn syrup. Vegetables were not included in his diet until he was 6 months of age, and he had at no time received iron in addition to that in his food. He had suffered no illnesses and had sat up alone at 5 months. A physical examination at the time of his admission for this study showed him to be

From the Department of Pediatrics of the University of Chicago School of Medicine.

This study was supported in part by a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

1. (*a*) Schlutz, F. W.; Morse, M., and Oldham, H.: The Influence of Fruit and Vegetable Feeding upon the Iron Metabolism of the Infant, J. Pediat. **3**:225 (July) 1933. (*b*) Oldham, H.; Schlutz, F. W., and Morse, M.: Utilization of Organic and Inorganic Iron by the Normal Infant, Am. J. Dis. Child. **54**:252 (Aug.) 1937.

healthy, well developed and normal in every respect. When he was 6½ months old his weight was 8,465 Gm. The hemoglobin content was 13 Gm. per hundred cubic centimeters of blood.

The study of the iron metabolism of this child was started when he reached the age of 7 months. In the eight months which followed, the amount of iron retained during six periods of six days each and twenty-five periods of three days each was determined. During the first six periods a metabolism frame was used for the collection of excreta. In this portion of the study the child received a given diet for at least a week before collections were made. Excreta were then collected for three periods of six days each, with intervals of three to seven days (between the periods) without collections. The diet was then supplemented with vitamin B_1, and the collection procedure was repeated for three additional six day periods.

After a period of training, the study was resumed for twenty-five periods of three days each. The collection of urine was discontinued, and a nursery chair with a harness was used for the collection of feces. Collections were as nearly continuous as possible, and the immediate effects of changes in the diet were observed, as well as those appearing after adjustment to the new diet.

During the eight months over which the study extended, two interruptions occurred owing to infections of the upper respiratory tract. One infection was severe, and otitis media developed. The other was moderately severe and resulted in no complications. Collections were discontinued at the onset of the infections and were not resumed until the child had recovered completely and had been eating normally for at least a week. With these exceptions the infant was in perfect health during the entire period of hospitalization.

The diet given was similar both in character and in proportion to that of any child of this age. The different foods which were included and the amount of each given daily are listed in table 1. The basic diet used throughout the study consisted of powdered milk,[2] cane sugar, cereal,[3] strained vegetables,[4] orange juice and cod liver oil. Strained fruit[5] was introduced when the child was 9 months of age.

The diet was reenforced by supplements of copper, iron and vitamin B_1. Cupric sulfate, in amounts which furnished 0.1 mg. of copper per kilogram of body weight, was included in the diet as a matter of routine to insure an optimum intake of that mineral. The iron intake was raised to the desired levels by the addition of varying amounts of ferric pyrophosphate to the daily formula. Supplements of vitamin B_1[6] were included in the diet in certain periods of the study and were omitted in control periods.

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2. Powdered milk in the form of Dryco was furnished by the Borden Company.

3. Farina, a purified wheat cereal, was used throughout the study.

4. Strained vegetables were furnished by Clapp's, Inc. Peas, green beans and asparagus were used in rotation during the entire study.

5. Strained fruits were furnished by Clapp's, Inc. Apricots and prunes were given daily.

6. A supply of crystalline vitamin B was furnished by Merck and Co., Inc. Ten milligrams of the crystals was dissolved in 250 cc. of distilled water to which small amounts of hydrochloric acid and alcohol had been added to prevent deterioration of the vitamin. The amount given daily was approximately 10 international units per kilogram of body weight.

It will be noted (table 1) that it was occasionally necessary to make changes in the diet within a group of periods when it would have been more desirable to keep the intake constant. The amount of fruit was increased at the beginning of period 10 in order to prevent constipation. During later periods the child's appetite varied considerably. In period 13 it was apparent that he was not satisfied after his meals. Since the cereal contributed the least amount of iron, the amount given was increased at the beginning of period 14. After four periods of the higher intake the appetite lessened, and appreciable quantities of cereal

TABLE 1.—*Dietary Intake*

Period No.	Daily Diets	Deviations from Basal Diet
1-3	Basal diet 1* Ferric pyrophosphate (1.3 mg. iron) Cupric sulfate (0.9 mg. copper)	
4-6	Basal diet 1 Ferric pyrophosphate (1.3 mg. iron) Cupric sulfate (1 mg. copper) 90 international units vitamin B_1	
7-11	Basal diet 1 50 Gm. strained apricots 20 Gm. strained prunes Ferric pyrophosphate (3.77 mg. iron) Cupric sulfate (1 mg. copper)	Prunes increased to 30 Gm. in periods 10 and 11
12-16	Basal diet 1 50 Gm. strained apricots 30 Gm. strained prunes Ferric pyrophosphate (3.77 mg. iron) Cupric sulfate (1 mg. copper) 108 international units vitamin B_1	Cereal increased to 30 Gm. in periods 14 to 16
17-21	Basal diet 2† 70 Gm. strained apricots 30 Gm. strained prunes Ferric pyrophosphate (5.78 mg. iron) Cupric sulfate (1.1 mg. copper) 108 international units vitamin B_1	Cereal intake irregular; 30, 27, 18, 20 and 13 Gm., respectively, during periods 17 to 21
22-26	Basal diet 2 70 Gm. strained apricots 30 Gm. strained prunes Ferric pyrophosphate (5.75 mg. iron) Cupric sulfate (1.1 mg. copper)	Cereal intake 13 Gm. in period 22; 20 Gm. in periods 23 to 26; sugar decreased to 30 Gm. in periods 23 to 26
27-31	Basal diet 2 70 Gm. strained apricots 30 Gm. strained prunes Ferric pyrophosphate (5.78 mg. iron) Cupric sulfate (1.1 mg. copper) 126 international units vitamin B_1	Cereal 20 Gm. and sugar 30 Gm. in periods 27 to 31

* Basal diet 1 consisted of 115 Gm. powdered milk, 45 Gm. cane sugar, 8 cc. cod liver oil, 60 cc. orange juice, 20 Gm. cereal and 70 Gm. strained vegetable.

† Basal diet 2 was similar to basic diet 1 with the exception that the vegetables were increased to 100 Gm.

were refused during periods 18 to 22. An interruption occurred between periods 22 and 23, owing to a moderately severe infection of the upper respiratory tract. After recovery, the amount of sugar in the diet was decreased, and the intake of cereal was constant at the lower level for the remainder of the study.

The general details regarding the treatment of the food, as well as the precautions observed to prevent contamination of food and excreta, were similar to those reported in a previous study.[1b]

The iron metabolism was observed at three levels (approximately 0.5, 0.8 and 1.2 mg. per kilogram) of iron intake. Iron was given at each level for fifteen

days or more with a fairly low intake of vitamin B_1[7] (approximately 10 units per kilogram) and for a comparable length of time with a higher intake (approximately 20 units per kilogram). During the time the child was receiving 0.5 and 0.8 mg. per kilogram of iron, the vitamin B_1 intake was increased after collections had been made at the lower level. At the higher level of iron intake, of 1.2 mg. per kilogram, supplements of vitamin B_1 were given both before and after the control periods with the lower vitamin B_1 level. Since the child had previously become adjusted to the higher level of vitamin B_1 it was thought that a continuation of this same high level would eliminate any complications occurring as the immediate effect of an increased vitamin intake and that it might result in retention comparable to that found during the control periods. Any immediate effect of an increased intake of iron would also be eliminated in the control periods by this procedure.

The total iron content of both food and excreta was determined by a modification of Stugart's method,[8] which has been described elsewhere.[1] No attempt was made to determine the inorganic iron content of the food, since the greater part of the iron in the diet was supplied by foods which contain practically no organic iron and by ferric pyrophosphate, which is completely in the inorganic form.

Calcium retention was ascertained during the periods in which both urine and feces were collected. The method of Fiske and Logan[9] was used to determine the amount of calcium in food and excreta.

The hemoglobin content was determined by the Newcomer method.[10] Three determinations were made on successive days prior to a change in the diet, and average values were used.

RESULTS

The average retention of iron for the different levels of intake of iron, both with and without additional vitamin B_1, is shown in table 2 and chart 1. A lower average retention was found in each group of periods representing increased intake of the vitamin (series B, D, E and G) than in similar groups of periods in which the intake was lower (series A, C and F). When the iron intake was more than 1 mg. per kilogram (series E, F and G) the differences in retention between the periods of high vitamin intake (series E and G) and the control periods (series F) were smaller. However, since the average retention in the two series with high vitamin B_1 intake at this higher level of iron intake was the same and was less than that of the control series (0.018 and

7. Dr. Elizabeth Knott assayed composites of food which represented average diets for one day. The daily intake of vitamin B_1 from the food was found to range from 90 to 120 international units, or approximately 10 units per kilogram of body weight.

8. Stugart, R.: Determination of Iron in Milk and Other Biological Materials, Indust. & Engin. Chem. (Analyt. Ed.) **3**:390 (Oct.) 1931.

9. Fiske, C. H., and Logan, M. A.: The Determination of Calcium by Alkalimetric Titration: II. The Precipitation of Calcium in the Presence of Magnesium, Phosphate and Sulfate, with Applications to the Analysis of Urine, J. Biol. Chem. **93**:211 (Sept.) 1931.

10. Newcomer, H. S.: A New Optical Instrument for the Determination of Hemoglobin, J. Biol. Chem. **55**:569 (April) 1923.

TABLE 2.—*Average Intake and Retention of Iron*

Series	Periods	Number of Days	Diet	Average Intake, Mg. per Kg. per Day	Average Retention, Mg. per Kg. per Day
A	1-3	18	Basal	0.48	+0.020
B	3-6	18	Basal + B_1	0.42	—0.012
C	7-11	15	Basal + fruit	0.82	+0.046
D	12-16	15	Basal + fruit + B_1	0.82	—0.001
E	17-21	15	Basal + fruit + B_1	1.08	+0.019
F	22-26	15	Basal + fruit	1.32	+0.030
G	27-31	15	Basal + fruit + B_1	1.23	+0.018

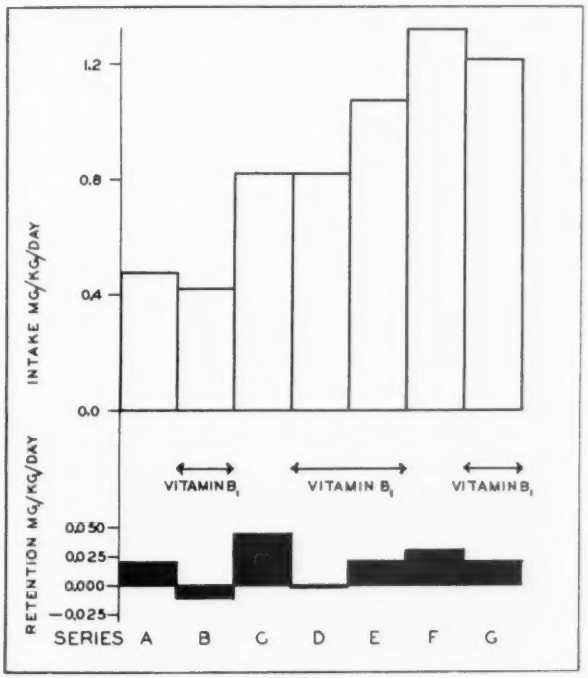

Fig. 1.—Average retention of iron as influenced by supplements of vitamin B_1.

0.019 mg. per kilogram, as compared with 0.03 mg. per kilogram), even these smaller differences may have significance. The decreased effect of vitamin B_1 observed at the higher level of iron intake may have been either a result of that higher level or of an increased capability of adjustment to the higher intake of vitamin B_1 as the child grew older.

Variations in retention which occur from period to period within a series are sometimes obscured when only the average retention is considered. The intake and retention of iron for the individual periods are given in table 3 and are represented graphically in chart 2.

During periods in which the intake of vitamin B_1 was at the higher level, variations occurred in the retention found in individual periods

TABLE 3.—*Daily Intake and Retention of Iron for Individual Periods*

Series	Period	Age	Weight	Iron Intake, Mg.	Iron Intake, Mg. per Kg.	Supplementary Vitamin B_1, International Units	Weight of Feces, Gm.	Retention, Mg. per Kg.
A	1	28	8.8	4.41	0.50	...	13.46	+0.044
	2	30	9.0	4.33	0.48	...	11.37	+0.008
	3	31	9.2	4.19	0.46	...	12.62	+0.008
B	4	33	9.5	3.97	0.42*	90	10.80	−0.008
	5	35	9.6	3.91	0.41	90	11.79	−0.001
	6	36	9.8	4.07	0.42	90	12.19	−0.028
C	7	44	10.0	8.21	0.82	...	13.14	+0.051
	8	44	10.0	8.34	0.83	...	13.11	+0.042
	9	45	10.1	8.09	0.80	...	12.81	+0.049
	10	45	10.1	8.37	0.83	...	14.28	+0.009
	11	46	10.2	8.48	0.83	...	13.15	+0.079
D	12	46	10.3	8.70	0.84	108	13.44	−0.161
	13	47	10.4	8.37	0.80	108	13.44	+0.038
	14	47	10.4	8.54	0.82	108	14.59	−0.001
	15	48	10.5	8.96	0.85	108	14.65	+0.070
	16	48	10.7	8.49	0.79	108	14.26	+0.061
E	17	49	10.9	11.39	1.04	108	14.99	+0.052
	18	49	10.9	11.20	1.03	108	14.87	−0.042
	19	50	11.0	10.98	1.00	108	13.87	+0.073
	20	50	11.0	12.43	1.13	108	14.70	−0.026
	21	51	11.1	13.23	1.19	108	14.26	+0.038
F	22	51	11.0	14.99	1.36	...	14.19	+0.074
	23	55	10.9	14.45	1.33	...	14.54	−0.008
	24	56	11.1	13.81	1.26	...	13.89	+0.002
	25	56	11.1	14.79	1.33	...	13.88	+0.005
	26	57	11.1	14.74	1.33	...	13.34	+0.076
G	27	57	11.1	14.46	1.30	126	13.22	+0.005
	28	58	11.1	15.14	1.36	126	14.78	−0.002
	29	58	11.1	12.90	1.16	126	13.65	+0.004
	30	58	11.1	13.50	1.18	126	12.90	+0.039
	31	59	11.1	13.12	1.14	126	13.33	+0.045

* Three factors contributed an additive effect to the reduction of the intake of iron in periods 4 to 6, namely: (1) rapid gain in weight, (2) variability in the iron content of the orange juice and (3) the refusal of small amounts of food.

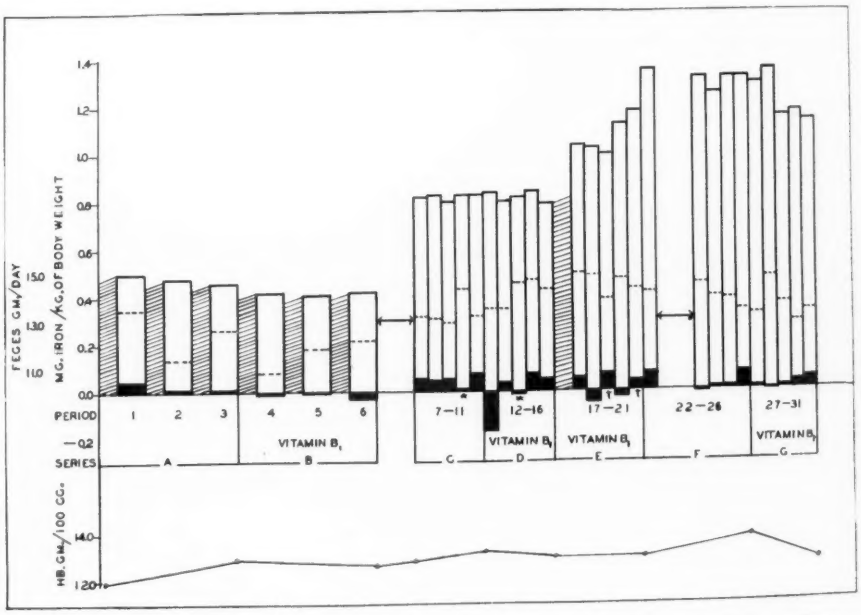

Fig. 2.—The intake of iron for each period is represented by the entire column and the corresponding retention by the black portion. The dotted line across each column represents the dry weight of the feces for that period. The cross-hatched portions represent intervals of less than a week with a given diet before collections were made, and the arrows indicate interruptions in the study. The hemoglobin values are also shown. The asterisk indicates an initial period of increased bulk. The dagger indicates an initial period of decreased bulk.

which may have significance. In series B, in which the vitamin intake was increased eight days before collections were made, a small negative iron balance was found during each period. In series D, in which collections were begun at the same time that the vitamin intake was increased, a large negative balance was observed in period 12 and a small negative balance in period 14, but positive balances were observed in all other periods. In series E, in which any immediate effect of the increased intake of vitamin B_1 was eliminated (since a similar intake in the previous series had given opportunity for adjustment), the iron balance was irregular. No large negative balance was noted, such as was found in the first period of series D. In series G, in which collections were again started simultaneously with the increased intake of vitamin B_1 a small retention of iron was found during the first three periods, but, again, there was no large negative balance. The retention during the last two periods of series G was higher. A comparison of the results of series D and G with those of series B suggests that the increased capability of adjustment to the higher level of vitamin B_1 found as the study progressed might have been due to several factors, such as the increased age of the child, the higher intake of iron and the fact that the child had previously received a considerable amount of vitamin B_1.

Considerable variation in the iron retention was found with the higher levels of iron intake. These variations seem to have resulted from an inability on the part of the child to adjust immediately to slight changes in the amount of food consumed, rather than from any variation in the iron intake. In period 10 an increased fecal weight and a lowered retention of iron were coincident with a slight increase in the amount of prunes included in the diet. In periods 14 and 22, the intake of cereal was higher than that in previous periods, and the fecal weight was higher, while the retention was again lowered noticeably. Conversely, during initial periods of decreased intake of cereal (periods 19 and 21) the fecal weight was lower and retention was higher than during the periods immediately preceding. These variations in retention could not have been due to variations in fecal weight only, for differences in fecal weight also occurred during periods in which both food consumption and iron retention remained at a constant level.

The hemoglobin content of the blood was in the high normal range (12 to 14 Gm. per hundred cubic centimeters) and remained fairly constant. Slight decreases occurred during each series in which there was an increased intake of the vitamin, and slight elevations during each control series. These differences, however, were small and are not considered significant.

It seems that the data which have been presented confirm our previous finding concerning the influence of vitamin B_1 on the retention

of iron, namely, that the vitamin tends to have an unfavorable influence on the iron balance, at least in initial periods. This effect of vitamin B_1 is surprising, and at present we can offer no explanation. Further investigation is now in progress in which wider ranges in the intake of vitamin B_1 are being made possible by the use of animals as experimental subjects.

The retention of calcium was determined during periods 1 to 6. It may be noted in table 4 that an increased excretion of calcium in the urine occurred during the periods in which the intake of vitamin B_1 was at the higher level. The average retention of calcium remained approximately the same on the two levels of intake of vitamin.

It is interesting to compare the retention of iron found in this study with that reported in a previous study of a normal child of the same age. On the whole, the intake was lower and the retention higher

TABLE 4.—*Calcium Balance During the First Six Periods* *

Series	Period	Intake, Mg.	Output in Urine, Mg.	Output in Feces, Mg.	Retention, Mg.
A	1	154	2.84	116	+35.2
	2	147	2.67	110	+34.3
	3	140	2.28	105	+32.7
Average		147	2.60	110	+34.1
B	4	138	4.11	96	+37.9
	5	137	5.10	101	+30.9
	6	135	5.51	101	+28.5
Average		137	4.91	99	+32.4

* Results are expressed in milligrams per kilogram of body weight.

and less variable in the case of the infant studied previously. His average retention with an intake of less than 0.4 mg. per kilogram was comparable to the average retention found in the infant observed in this study with an intake of 0.82 to 1.32 mg. per kilogram. With a slightly higher intake (0.47 mg. per kilogram), his retentions averaged 0.07 mg. per kilogram, as compared to the average retention of 0.02 mg. per kilogram shown by the infant of the present study with a similar intake (0.48 mg. per kilogram). In a comparison of the nutritive status of the 2 infants, only one difference is apparent. The hemoglobin content of the infant studied previously was 9 to 11 Gm. per hundred cubic centimeters of blood, while that of the infant of this study was 12 to 14 Gm. per hundred cubic centimeters. It is possible that the greater need for iron on the part of the child having the lower hemoglobin value may have resulted in the retention of comparatively larger amounts of iron.

There is no evidence that this child required more than 0.8 mg. of iron per kilogram per day for optimum retention. This is slightly

lower than the 1 mg. recommended by Stearns and Stinger.[11] However, since the hemoglobin content of the blood of this child was higher than that of the average normal child of the same age, the allowance of 1 mg. of iron per kilogram per day is probably justifiable.

SUMMARY

The influence of vitamin B_1 on the iron metabolism of a normal child was studied at three levels of iron intake. Iron at each level of intake was given both with and without supplements of crystalline vitamin B_1.

The average retention of iron was lower during periods of high vitamin B_1 intake than during the control periods, although the differences were less as the study progressed. It is suggested that the child acquired an increased capability to adjust to the higher vitamin intake as he grew older.

For the most part, variations in the retention with a given diet were correlated with the amount of food consumed rather than with the intake of iron. With a relatively constant intake of iron, an increase in consumption of food resulted in a lower retention of iron, and a decrease resulted in a higher retention.

These results substantiate our previous findings as to the influence of vitamin B_1 on the retention of iron.

An increased excretion of calcium in the urine was found coincident with an increase in the level of intake of vitamin B_1 in the periods during which the retention of calcium was determined. Calcium retention was not affected by the higher level of vitamin B_1.

No evidence was shown that this child required more than 0.8 mg. of iron per kilogram per day for optimum retention, although a higher allowance may be justifiable. There is apparently an individual variation in retention of iron which may be accounted for by the hemoglobin concentration of the blood.

11. Stearns, G., and Stinger, D.: Iron Retention in Infancy, J. Nutrition **13**:127 (Feb.) 1937.

CERVICAL RIB IN EARLY LIFE

DAVID BENNETT DAVIS, M.D.
NEW YORK
AND
J. CASH KING, M.D.
MEMPHIS, TENN.

In the latter half of the year 1936, 3 children with cervical rib were seen at the John Gaston Hospital and at the outpatient clinic for diagnosis and treatment. This succession of cases within so short an interval of an entity usually described as producing symptoms only in adults suggested the possibility that similar cases might previously have been overlooked. It led to a review of 1,000 consecutive roentgenograms of the chests of children under 13 years of age taken at the John Gaston Hospital and at the outpatient clinic beginning Jan. 1, 1936. The result of this review and the reports of the 3 cases observed are incorporated in this paper, together with a general discussion of cervical rib in early life.

Cervical rib was first described, long ago, by Galen and Vesalius, and since their time many and prolific have been the writers who have observed this anomaly and have recorded their observations in the literature. Worthy of mention are the contributions of Hunauld [1] in 1740, Murphy [2] in 1906, Keen [3] in 1907, Todd [4] in 1911, Jones [5] in 1915,

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From the Department of Pediatrics and the Department of Radiology, University of Tennessee School of Medicine.

1. Hunauld: Sur le nombre des côtes, moindre ou plus grand qu'a l'ordinaire, Hist. Acad. roy. d. sc., Mém., 1740, pp. 534-539.

2. Murphy, J. B.: The Clinical Significance of Cervical Ribs, Surg., Gynec. & Obst. **3**:514-520, 1906.

3. Keen, W. W.: The Symptomatology, Diagnosis and Surgical Treatment of Cervical Ribs, Am. J. M. Sc. **133**:173-218, 1907.

4. Todd, T. W.: (*a*) Cervical Rib: Factors Controlling Its Presence and Its Sizes; Its Bearing on the Morphology of the Shoulder, with Four Cases, J. Anat. & Physiol. **46**:244-288, 1911-1912; (*b*) The Arterial Lesions in Cases of Cervical Rib, ibid. **47**:250-253, 1912-1913.

5. Jones, F. W.: The Anatomy of Cervical Ribs, Proc. Roy. Soc. Med. (Clin. Sect.) **6**:95-113, 1912-1913.

Henderson [6] in 1913, Halsted [7] in 1916, Southam and Bythell [8] in 1924 and Adson and Coffee [9] in 1927. Although occasional cases in which the condition occurred in early life have been reported by various authors, only Southam and Bythell limited their discussion solely to its occurrence in children, and we concur in the opinion of these writers that the incidence of cervical rib which produces symptoms in children is greater than is generally conceded and has not been given the consideration it deserves.

REPORT OF CASES

Case 1.—F. A., a 10 year old girl, was admitted to the John Gaston Hospital on Sept. 20, 1936. Her mother related that the child had had pain behind the left ear and in the left side of the neck for three years. This pain came on in sudden attacks at varying times and intervals. It was sharp and severe and radiated down through the shoulder to the left arm. During each attack the child kept her head bent and turned to the right side, saying that it was painful to move it to the left. There had never been any discharge from either ear. The child had wet the bed occasionally all her life, and since the onset of her present complaint she had become a constant bedwetter. The child's father and mother were both living and well. She had a sister, aged 12, who was well; and a brother, aged 6, who had asthma. Birth and development had been normal. She had been immunized against diphtheria and typhoid and had been vaccinated for smallpox. She had had measles, mumps, chickenpox, whooping cough and pneumonia. She had had occasional sore throats until tonsillectomy was performed in 1933.

Physical examination revealed a fairly well developed, poorly nourished girl who was not acutely ill or in intense pain. The temperature was 99 F., the pulse rate 90 and the respiratory rate 20. The hair and scalp were normal. The head was turned and bent slightly to the right at an angle of about 30 degrees (fig. 1). The patient would not turn the head to the left, saying that it caused her severe pain. Any effort at passively moving the head to the left was resisted.

The pupils were equal and regular and reacted normally to light and in accommodation. The extraocular muscles were normal. The vision was normal.

Both ear drums were normal. All landmarks were clearly visible. The external auditory canals were normal. There was some pain on movement of the left external ear, and there was slight mastoid tenderness on that side. This tenderness extended down over the neck to the shoulder. No cervical glands were

6. Henderson, M. S.: Cervical Rib: Report of Thirty-One Cases, Am. J. Orthop. Surg. **11**:408-430, 1914.

7. Halsted, W. S.: An Experimental Study of Circumscribed Dilation of an Artery Immediately Distal to a Partially Occluding Band, and Its Bearing on the Dilation of the Subclavian Artery Observed in Certain Cases of Cervical Rib, J. Exper. Med. **24**:271-286, 1916.

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9. Adson, A. W., and Coffee, J. R.: Cervical Rib, Ann. Surg. **85**:839-857, 1927.

palpable. The nose and throat were normal. The tonsils had been removed. There were several carious teeth.

The thorax was hyposthenic. The lungs were clear; the heart was normal.

The abdomen was soft. No masses were palpable. The liver, the spleen and the kidneys were not palpable. No tenderness was elicited over the renal regions.

The extremities were normal. The radial pulse was equal on the two sides.

A neurologic examination revealed no abnormality.

The laboratory examinations revealed no abnormality. A Kahn test of blood gave negative results. The Mantoux test also gave a negative reaction.

Roentgenograms of the mastoids, the cervical portion of the spine, the chest, the mandible and the temporomandibular joints showed them to be normal.

The child's symptoms cleared up spontaneously after several days without treatment, and she was discharged to the outpatient clinic for observation. The diagnosis was torticollis of undetermined origin.

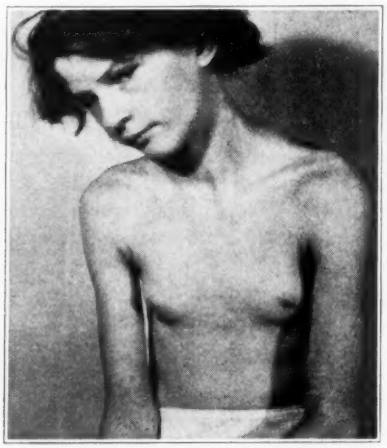

Fig. 1.—A photograph of F. A., showing her position in an attack of torticollis.

On October 1 the child returned to the hospital with an attack of acute appendicitis. Appendectomy was performed on the evening of her entry. Recovery was uneventful.

On November 14 the child was again admitted to the John Gaston Hospital, this time with the original complaint, that is, pain in the left side of the neck, with stiffness of the muscles and swelling on that side. The physical examination gave essentially the same results as on the first entry, except that, in addition to the torticollis, there was slight nonpitting edema of the left side of the neck. It was also noted that if the left arm was raised over the head and the head was turned sharply to the right, the left radial pulse could be obliterated. A roentgenogram of the neck, taken at this time, revealed a short cervical rib extending about 0.5 cm. past the end of the transverse process of the seventh cervical vertebra on each side. Dr. D. W. Carr, a specialist in thoracic surgery, was consulted. He agreed with the diagnosis of cervical rib but did not believe that surgical intervention was indicated until the child had been observed for a longer period. The child was sent back to school and was observed in the

outpatient clinic at frequent intervals. In December 1937 she said that she still had occasional attacks of torticollis and pain in the neck, which subsided only after a day of rest. However, she was getting along fairly well in school, and it was felt that surgical treatment could be deferred until the summer vacation.

CASE 2.—J. O., an 11 year old Armenian girl, had been seen in the outpatient clinic several times since she was 7½ years old, for minor complaints. On Aug. 28, 1936, she was again brought into the clinic by her mother, who stated that for the past six months the child had had frequent headaches associated with pain on the left side of the neck. The pain was severe and was accompanied by a swelling on the left side of the neck and by prominence of the blood vessels in that region. The attacks were not related to exercise or exposure. She also complained of nervousness and occasional attacks of palpitation.

The child's father and mother were both living and well. She had a sister and a brother, both living and well. Her birth history was normal. Her development was normal. She had been immunized against typhoid, diphtheria and smallpox. She had had measles, chickenpox and scarlet fever and had suffered occasional sore throats. She was in the fifth grade at school and was an apt pupil.

Physical examination revealed a well nourished and well developed girl who was in no pain or discomfort. She was intelligent and cooperative.

The hair and scalp were normal.

The vision was normal. The pupils were equal and regular and reacted to light and in accommodation. The extraocular muscles were normal. The ears, nose and throat were normal. The teeth were in good condition.

Examination of the neck revealed a fulness involving chiefly the left side and prominence of the veins on that side. The normal concave contour of the fold over the left trapezius muscle gave way to a convexity, and palpation of this convexity revealed a hard, bony mass of indefinite proportions. No glands were palpable.

The chest was hyposthenic. The heart and the lungs were normal. The abdomen, the back, the extremities and the genitalia were normal. The radial pulse was equal on the two sides. The left radial pulse could be obliterated by raising the left hand above the head and turning the head to the right. There was no difference in the temperature of the two upper extremities.

A neurologic examination elicited no abnormal findings.

A roentgenogram of the chest and neck revealed a cervical rib on the left, measuring approximately 1¼ inches (3 cm.) in length, lying close to the first thoracic rib.

After the patient had been observed for several months, it was noted that she had only occasional attacks of mild pain, which were relieved by rest. At this time we do not feel that surgical treatment is indicated. The patient will be kept under observation, and operation will be resorted to only if the severity of the symptoms warrants such a procedure. In the meantime, the child has been instructed in exercises to strengthen the muscles of the left side of the shoulder girdle.

CASE 3.—K. L., a 6 year old girl, was admitted to the John Gaston Hospital on Oct. 21, 1936. The informant was the child's aunt, who said that about three months previously she noticed that the child did not use the left hand while playing. On closer inspection she found that there was weakness of the wrist and of the fingers on that side and that the left hand seemed smaller than the right. After that no change was noted in the condition until three days before

entry, when the child complained of severe pain in the left arm. This pain had persisted up to the time she was brought into the hospital.

The child had had chickenpox but no other children's diseases. She was chronically constipated. She had had no immunizations. She was born by cesarean section, the mother dying shortly after the operation. The developmental history was normal.

The father was living and well. The grandfather had asthma. There was no family history of tuberculosis, syphilis or diabetes.

Physical examination revealed a well developed and well nourished girl who did not appear acutely ill or in severe pain.

The hair and scalp were normal. The skin was of normal texture and moisture.

The pupils reacted to light and in accommodation. The extraocular movements were normal. The conjunctivas were injected, and the lids were swollen from crying. The fundi were normal.

The mucous membranes of the nose were hyperemic. The left ear was normal. The membrane of the right ear drum was injected. The teeth were normal; there was no caries. The tongue and palate were normal. The tonsils were moderately hypertrophied, cryptic and inflamed.

There was a slight bulging in the left supraclavicular fossa, where a hard, rounded bony eminence was felt. A similar prominence was noted on the right but was not as large. There was no adenopathy.

The lungs were clear. The heart was normal. The blood pressure was 84 systolic and 56 diastolic in the right arm and 80 systolic and 52 diastolic in the left arm.

The abdomen was normal.

There was weakness of the left arm and hand, with definite atrophy of the muscles of the left arm and forearm and of the intrinsic muscles of the left hand (fig. 2). The left upper extremity did not feel as warm or as moist as the right. There was tenderness to deep pressure over the course of the nerves of the left arm. The radial pulse was of equal volume on the two sides, but when the left arm was raised above the head and the head was turned to the right, the left radial pulse would disappear.

Neurologic examination revealed weakness of all the muscles of the left arm and the left side of the shoulder girdle. Sensation was normal over this area, except that tenderness was elicited by deep palpation. The reflexes were normal and equal bilaterally.

The temperature was 99 F., the pulse rate 96 and the respiratory rate 18. The laboratory findings were within normal limits. The Kahn tests of both the blood and the spinal fluid gave negative results.

Roentgenologic examination revealed bilateral cervical ribs lying close to the first thoracic ribs. The long bones showed no significant changes.

Dr. D. W. Carr advised tenotomy of the scalenius anticus muscle on the left side. This was done on October 14. The convalescence was uneventful, and the patient left the hospital on the seventh day after the operation. She was entirely free from pain.

She was seen again on May 22, 1937, at which time it was learned that she still had occasional mild attacks of pain radiating down the left arm. Physical examination revealed no important change except that there was now no apparent difference in temperature between the two upper extremities. The grip of the left hand was still weak, and there seemed to be no improvement in the muscles of the forearm, the arm and the shoulder girdle.

COMMENT

The incidence of cervical rib has been variously estimated at between 0.03 and 0.1 per cent. In about 70 per cent of all cases it is bilateral, but in only 33.3 per cent even of these are bilateral symptoms observed. Symptoms more commonly affect the right side than the left. Symptoms appear more commonly in females than in males, the ratio varying from 3:1 to about 8:1 in different studies. The occurrence of cervical rib has been shown to have a definite familial tendency. The symptoms produced by this anomaly generally do not appear until late adolescent or early adult life. The delay in the production of symptoms by cervical

Fig. 2.—A photograph of K. L., showing atrophy of the left arm and forearm and the weak grip of the left hand.

rib until the second and third decades of life has been ascribed to three factors, namely, the delay in ossification of the rib, the delay in the completion of its growth and the delay in the descent of the shoulder girdle. The descent of the shoulder girdle is generally not complete until the twentieth year. Ossification and growth of the cervical rib are not complete until the twenty-fifth year. Should any or all of these stages of development occur prematurely, it follows that symptoms might be produced at an early age. It may be well here to call attention to the fact that because of the aforementioned delay in ossification a fairly large cervical rib may appear in the roentgenogram as only a small

nubbin, thus deceiving the observer as to its actual size and its potentiality as a source of pressure. It is well to remember, too, that the size of the cervical rib does not necessarily indicate the severity of the symptoms. A large rib may produce no ill effects, whereas a small one may cause severe symptoms.

The cervical rib takes origin embryologically from the center of ossification of the anterior root of the transverse process of the seventh cervical vertebra. This center generally appears at about the sixth month of fetal life. The fact that this embryonic structure does not normally progress to full development has been attributed to a variation in the normal arrangement of nerve plexuses. In lower forms of animal life, that is, in animals having no extremities, such as the snake, cervical and lumbar ribs are the rule. However, in the higher forms, in the course of whose development limb buds (the precursors of the extremities) appear, these cervical and lumbar ribs are usually eliminated. When these limb buds first appear, they cover several vertebral segments. The nerves from the segments originally grow outward at approximately right angles to the spinal column and into the limb buds. Then, as the vertebral column grows in its long axis and the limb buds do not keep pace, the segmental nerves are soon following an oblique course (rather than a straight one) to reach the buds. It is at this point that the conflict occurs between the nerves and the newly forming ribs, the large nerve trunks pressing on the comparatively small ribs, impeding their growth and stunting them so that they form merely vertebral transverse processes. Since the degree of development of a cervical rib depends on the nature of the obstruction in its path, it may be readily seen that if the nerve plexuses which normally resist its growth were to come off the vertebral column at a higher level, the rib would be free to grow and develop, just as in the lower forms of animal life.

A review of the anatomy of the cervical rib may shed some light on the manner in which it produces symptoms. To quote Adson and Coffee:[9]

> The complete cervical rib extends out laterally from the seventh lateral vertebral process for varying distances, then turns forward and downward between the Scalenus Anticus and Medius muscles to meet the costal cartilage of the first rib. As the rib turns downward, the brachial plexus passes over it; then on its downward course the subclavian artery arches backward and laterally over it. Usually the Scalenus Anticus has attached itself to the cervical rib as the rib has pushed forward. Still lateral to the rib and outside of the Scalenus Anticus arches the subclavian vein, lower than the artery. The muscle lies between the vein and the cervical rib. Above the vein and nearly over the rib, passing transversely across the shoulder, are to be found two branches of the Thyroid Axis, the Suprascapular and Transverse Cervical. Above these arteries, running in the same general direction, is the inferior belly of the Omohyoid muscle.

The phrenic nerve passes downward along the anterior border of the Scalenus Anticus; within the costal arch, usually out of danger, lies the carotid sheath, with the common carotid artery, the internal jugular vein, and the vagus nerve. Over all these structures, laterally and anteriorly runs the lower end of the sternocleidomastoid muscle, with the external jugular vein passing down its postero-external border.

Probably the most common symptom of cervical rib is tumor of the neck. Other symptoms may be divided into those of vascular and those of nervous origin. Interference with circulation is brought about chiefly by compression of the subclavian artery, either by the cervical rib itself, as the artery arches over it, or by the scalenus anticus muscle. Instances of pressure on the subclavian vein which produced aneurysm have been reported. Thrombosis of the vessels at the site of obstruction has been known to occur. Circulatory disturbances may become manifest in a number of ways, varying from mild changes in the color and temperature of the extremity involved to trophic changes or even gangrene of the fingers. The radial pulse may be diminished in volume or may be completely obliterated. In those cases in which the radial pulse is normal under ordinary conditions, if the arm on the affected side is raised over the head and the head is turned sharply to the opposite side, the pulse may be obliterated. This is known as the Halsted test and is explained by the stretching of the scalenus anticus muscle, with compression of the subclavian artery between the muscle and the cervical rib to which it is attached. Edema of the neck has been a prominent symptom in 2 of our cases and is probably due to pressure on the subclavian vein. Symptoms of nervous origin, such as pain, atrophy and sensory disturbances, are attributed to pressure on the brachial plexus. The pain associated with cervical rib may be dull and aching after a long day's work or play, or it may be sharp and knifelike when brought on by sudden turning of the head or shoulder. It is most commonly felt along the course of the ulnar nerve but may be felt along the distribution of the entire brachial plexus. It may or may not be associated with sensory disturbances, such as tingling and numbness. Atrophy is a late manifestation and may be limited to the intrinsic muscles of the hand or may involve any or all the muscles of the shoulder girdle, the arm, the forearm and the hand. Torticollis, or wryneck, is a frequent and prominent symptom of cervical rib in children. It is spasmodic and is caused by pressure on the spinal accessory nerve. Spasmodic torticollis was present in 5 of 9 children in the cases reported by Southam and Bythell [8] and was also the outstanding feature of 1 of our cases. The association of Horner's syndrome with cervical rib has been described; it is presumably due to pressure or traction on the inferior cervical ganglion. Symptoms of pressure involving the vagus and the recurrent laryngeal nerves are other rare complications.

The diagnosis depends chiefly on the roentgenologic studies; but a careful history and an accurate evaluation of the symptoms, together with the finding of tumor of the neck associated with nervous and vascular changes in the upper extremity, as previously described, should lead the clinician to a provisional diagnosis even before the roentgenogram has been taken. Roentgenologic diagnosis usually presents little difficulty. With children in whom the rib is small and is not readily visualized in the usual roentgenograms of the chest, oblique views in which the rays are directed upward, laterally and posteriorly toward the affected side will demonstrate more clearly the full length of the

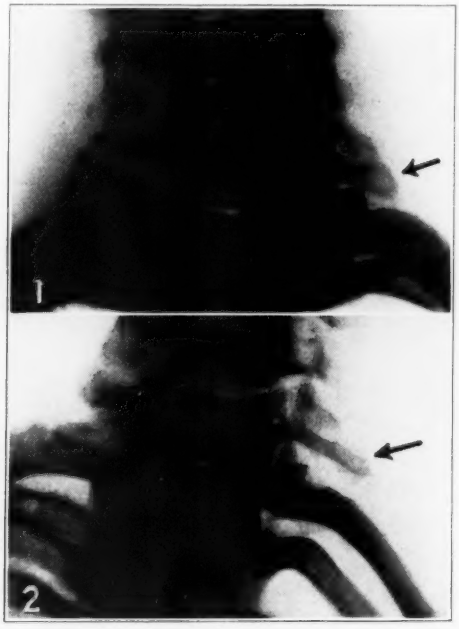

Fig. 3.—Two roentgenograms taken of the same child. Roentgenogram 1 was taken by the usual posteroanterior technic. Roentgenogram 2 was taken by the oblique method suggested. A comparison of the two demonstrates clearly the value of the oblique view in bringing out the true proportions of the cervical rib.

rib. The taking of roentgenograms by this method is recommended in the study of a cervical rib before surgical treatment is advised (fig. 3).

The treatment of cervical rib is operative, but since in the majority of cases of this anomaly there are no symptoms it is well to observe a patient long and thoroughly before resorting to surgical intervention. Three good rules to follow are: 1. Never inform a patient of the presence of a cervical rib that is not producing symptoms; certain patients, once informed, are forever conscious of it and acquire neurotic tendencies. 2. Advise surgical treatment only in cases in which the

nervous or vascular disturbance is sufficient to incapacitate the patient. 3. If surgical intervention is indicated, operate early and avoid permanent damage to the tissues involved.

The surgical procedure of choice seems to lie between complete excision of the rib and tenotomy of the anterior scalenus muscle. Adson and Coffee [9] have stressed the advantages of the latter operation, but Patterson,[10] after pointing out that many variations exist in the anatomy of the neck wrote:

> Because of these variations I do not believe we can set down a single procedure which, when carried out, will relieve every case of so-called surgical rib. Simple division of the scalenus anticus has been advocated by some as being the operation of choice for all cervical ribs. I believe we must deal with the variations as we find them at the time of operation.

Observations Made in a Study of Twelve Cases of Cervical Rib in Children

Case Number	Patient	Age, Years	Sex	Race	Cervical Rib, Unilateral or Bilateral	Symptoms	Symptoms Incapacitating
1*	F. A.	10	F	W	Bilateral	Unilateral, left	Yes
2*	J. O.	11	F	W	Unilateral, left	Unilateral, left	No
3*	K. L.	6	F	W	Bilateral	Unilateral, left	Yes
4	K. F.	5	F	W	Unilateral, left	None	No
5	H. B.	12	F	N	Bilateral	None	No
6	W. M.	3	M	N	Bilateral	None	No
7	N. C.	2	F	W	Bilateral	None	No
8	B. H.	4	M	W	Bilateral	None	No
9	M. J.	11	F	W	Bilateral	None	No
10	R. S.	6	F	W	Bilateral	None	No
11	M. T.	8	F	N	Bilateral	None	No
12	S. L.	11	F	N	Bilateral	None	No

* Cases reported in text.

In borderline cases nonoperative treatment may be resorted to for a reasonable length of time. This consists of exercise aiming at the development of the muscles of the shoulder girdle.

The incidence of cervical rib in the 1,000 consecutive roentgenograms reviewed by us was 1.2 per cent, and because of the great discrepancy in the incidence given by previous writers and that which occurred in our series we are presenting reproductions of the roentgenograms in the 12 cases found (fig. 4).

The significant points regarding the series reviewed may be found in the accompanying table. In addition to the facts listed, two other pertinent factors noted in the study might be mentioned. First, every patient with cervical rib had a long neck and a hyposthenic thorax. Second, a marked variation was noted in the size and contour of the anterior root of the transverse process of the seventh cervical vertebra. In many instances it reached such proportions that it was difficult to

10. Patterson, R. H.: Surgery for Cervical Ribs, Ann. Surg. **102**:972-979, 1935.

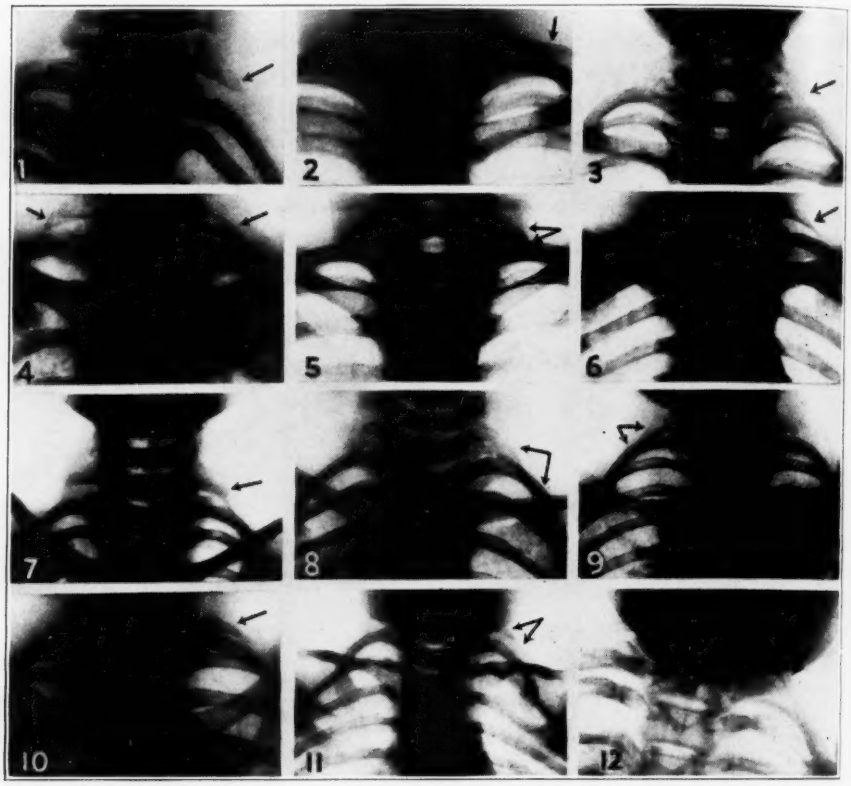

Fig. 4.—Reproductions of the twelve roentgenograms taken in our series of children with cervical rib. The first three plates in the top row, from left to right, are those of F. A., J. O. and K. L., respectively. These were the only children in the series in whom symptoms were produced.

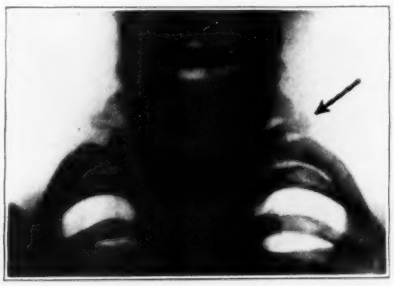

Fig. 5.—Roentgenogram taken of a child 4 years of age. The arrow points to a separate center of ossification adjacent to the transverse process of the seventh cervical vertebra. By the sixth year this may unite with the vertebra to form an elongated anterior root of the transverse process or, by persisting separately, may grow anteriorly and laterally, later to articulate with the vertebra and form a cervical rib.

differentiate it from a rudimentary cervical rib. This may be explained by the developmental anatomy of the seventh cervical vertebra. To quote Gray.[11]

> The anterior or costal part of the transverse process of this vertebra is sometimes ossified from a separate center which appears about the sixth month of fetal life and joins the body and posterior part of the transverse process between the fifth and sixth years. Occasionally the costal part persists as a separate piece and, becoming lengthened laterally and forward, constitutes what is known as a cervical rib.

Therefore, in the interpretation of roentgenograms of children under 5 years of age, the presence of a separate piece of bone adjacent to the transverse process of the seventh cervical vertebra should be recognized as a center of ossification, which is a potential precursor of a cervical rib (fig. 5).

SUMMARY

The cases of 3 children with cervical rib which produced symptoms are reported.

The incidence, embryology, anatomy, symptomatology, diagnosis and treatment of cervical rib are discussed.

The observations made in a study of 1,000 consecutive roentgenograms of the chest made on children under 13 years of age are recorded.

Reproductions of the twelve roentgenograms showing the cervical ribs found in the review are presented.

CONCLUSIONS

1. The incidence of cervical ribs which produce symptoms in children is greater than is generally known. The diagnosis will be made more frequently if the symptom complex is borne in mind.

2. Oblique roentgenograms of the neck and the upper part of the chest taken with the rays directed upward, laterally and posteriorly through the seventh cervical vertebra, will demonstrate more clearly the actual proportions of the rib.

3. In the interpretation of roentgenograms of children under 5 years of age, the presence of a separate piece of bone adjacent to the transverse process of the seventh cervical vertebra should be recognized as a center of ossification which is a potential precursor of a cervical rib.

11. Gray, H.: Anatomy, Descriptive and Applied, ed. 21, edited by W. H. Lewis, Philadelphia, Lea & Febiger, 1924, pp. 99-100.

PERMEABILITY OF BLOOD-CNS BARRIER TO SODIUM BROMIDE IN EXPERIMENTAL POLIOMYELITIS

EDWIN H. LENNETTE, M.D.
AND
DAN H. CAMPBELL, PH.D.
CHICAGO

The concentration of the normal constituents of the cerebrospinal fluid is a reflection of their concentration in the blood, changes in the latter concentration leading to corresponding changes in the spinal fluid. On the other hand, when foreign substances are introduced into the blood stream, they either fail to reach the spinal fluid or reach it in small amounts. This apparently does not depend on diffusibility, since some substances, such as iodides, ferrocyanides and phenosulfonphthalein, cannot be detected in the spinal fluid even when large amounts are administered intravenously,[1] whereas certain other substances, such as salicylates and bromides, are easily demonstrable in the spinal fluid shortly after enteric or parenteral administration.

Any substance, however, which alters the composition of the cerebrospinal fluid is rapidly eliminated when introduced into the subarachnoid space. Hence, while the passage of substances from the cerebrospinal canal into the general circulation is apparently unhindered, passage of the same substances in the opposite direction appears to be under the control of a regulating mechanism. This regulating mechanism, which is regarded as a functional entity[2] composed of various structures of the cerebrospinal nervous system, is usually referred to as the blood-brain (or blood-CNS[3]) barrier. The function of this barrier apparently is to maintain a physiologically constant composition of the cerebrospinal fluid and to exclude substances present in the blood stream which may be injurious to nerve tissue. When this barrier is damaged,

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From the Department of Bacteriology and Parasitology, University of Chicago.

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1. Cestan, Laborde and Riser: Presse méd. **33**:1330, 1925.

2. Katzenelbogen, S.: The Cerebrospinal Fluid and Its Relation to the Blood, Baltimore, Johns Hopkins Press, 1935.

3. Lennette, E. H., and Hudson, N. P.: Proc. Soc. Exper. Biol. & Med. **34**:470, 1936.

as in meningeal disorders, its permeability is altered.[4] As changes in the permeability of the blood-CNS barrier are known to occur in a number of pathologic conditions involving the central nervous system,[2] a change in the permeability of the barrier might also be expected in cases of poliomyelitis. If the alteration is in the direction of an increased permeability, its bearing on serum therapy or chemotherapy is obvious.

Lennette and Reames,[5] using the nitrate test of Mestrezat and Gaujoux,[6] obtained results which suggested that increased permeability of the barrier to NO_3^- may occur in experimental poliomyelitis; but the test is so crude and the results so variable [7] that evaluation of the findings is difficult. For this reason we had recourse to a more elaborate and more widely used method for determining alterations in the permeability of the barrier, the Walter bromide test.[8] With this method the concentration of bromide in the serum and in the spinal fluid is determined after oral administration of sodium bromide; the degree of permeability is represented by a ratio $\frac{\text{sodium bromide in serum}}{\text{sodium bromide in spinal fluid}}$, which is expressed as the permeability quotient. We[9] previously reported that an increased permeability of the barrier to Br^- occurs in experimental poliomyelitis; at this time we wish to present additional data.

MATERIAL AND METHODS

Animals.—Monkeys (*Macaca mulatta*) were used in all the experiments.

Virus.—The potent MV strain of virus was employed throughout this work.

Preparation of Animals.—Walter's original method was modified here, the sodium bromide being administered subcutaneously rather than orally. Each injection consisted of 45 mg. of sodium bromide per kilogram of body weight, the injections being given twice daily for two consecutive days. Specimens of blood and of spinal fluid for analysis were obtained approximately eighteen hours after the last injection. By this method of preparation it was found that the amount of sodium bromide in the body fluids mentioned varied roughly from 20 to 50 mg. per hundred cubic centimeters.

Specimens for Analysis.—While the animals were under ether anesthesia, blood was obtained by cardiac puncture, 5 cc. being withdrawn and allowed to clot in sterile tubes. Spinal fluid was obtained by cisternal puncture. The position of the animal was important, as it affected both the facility with which the cistern was entered and the avoidance of bloody fluids. After the neck had been

4. Katzenelbogen,[2] Flexner, S., and Amoss, H. L.: J. Exper. Med. **25**: 525, 1917. Lennette, E. H.: To be published.

5. Lennette, E. H., and Reames, H. R.: Proc. Soc. Exper. Biol. & Med. **36**: 769, 1937.

6. Loberg, K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:164, 1926.

7. Lennette, E. H., and Reames, H. R.: J. Immunol. **34**:215, 1938.

8. Walter, F. K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:522, 1925.

9. Lennette, E. H., and Campbell, D. H.: Science **86**:160, 1937.

shaved, the animal was anesthetized and placed on its abdomen, and the shaved area was cleansed with alcohol. An assistant strongly flexed the head on the chest, at the same time compressing the jugular veins against the vertebral column. The operator then inserted a sharp needle (1 inch [2.5 cm.], no. 20 or 22 gage, attached to a small syringe) vertically almost its entire length. Penetration into the cistern was marked by a sudden release of resistance and a gush of fluid into the syringe. By this procedure we were able to obtain routinely at least 2 cc. of fluid. Cisternal puncture always preceded withdrawal of blood, since hemorrhage tends to decrease the pressure of the cerebrospinal fluid.

Analysis of Blood and Spinal Fluid for Bromide.—That the detection of Br^- is interfered with to some extent by the presence of Cl^- is well known; a preliminary study therefore was made to determine to what degree this occurred and to ascertain whether the effect of the chloride could be satisfactorily eliminated. By determining the amount of sodium bromide detectable when constant amounts (50 mg. per hundred cubic centimeters) of bromide were added to solutions of sodium chloride of varying concentration (0 to 0.9 per cent), values were obtained which are shown in chart 1. It will be noted that when

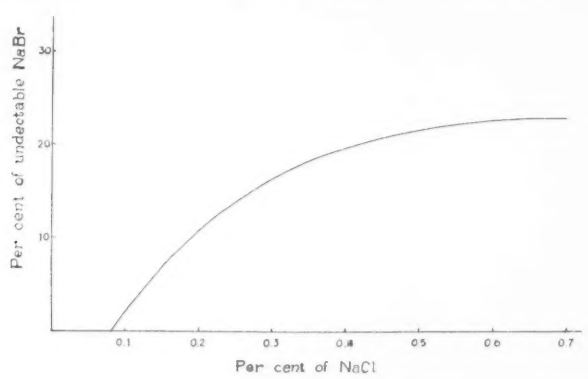

Chart 1.—Interference of sodium chloride in determination of sodium bromide.

the concentration of sodium chloride reaches approximately 0.05 per cent practically all the sodium bromide is detectable. It is possible, therefore, to dilute serum or spinal fluid to a point where the chloride effect is eliminated. Obviously, the initial concentration of sodium bromide must be sufficiently high to allow of this dilution; any original concentration above 10 mg. per hundred cubic centimeters makes this method feasible.

The procedure used for the determination of sodium bromide was as follows: To 1 cc. of serum, spinal fluid or standard solution of sodium bromide were added 1.4 cc. of distilled water and 0.6 cc. of a 20 per cent solution of trichloroacetic acid. The solutions were mixed well, allowed to stand at room temperature for one hour and centrifuged until the supernatant fluid was clear. One cubic centimeter of the supernatant solution was then added to 1.5 cc. of distilled water and 0.5 cc. of a 0.05 per cent solution of acid yellow gold chloride. After the fluids were mixed well, the unknowns were compared with standard solutions of sodium bromide in a Klett biocolorimeter with microattachments.

Our methods of chemical analysis differ in several respects from those used by Walter and others, the modifications being necessary to adapt the analytic procedures to the small amounts of spinal fluid obtainable from monkeys.

RESULTS

The permeability of the blood-CNS barrier to sodium bromide was studied in 127 monkeys, which were divided into 11 groups based on the type of material inoculated, the route of inoculation and the clinical condition of the animal. The permeability quotients and their statistical significance have been summarized in table 1.

The permeability quotient for 52 monkeys which showed typical symptoms of experimental poliomyelitis tended to fall around 1 in both the preparalytic and paralytic stages of the disease. No difference in quotient was found between animals infected by the intracerebral route and those infected by the intranasal route. The permeability quotients for 29 animals which were inoculated with virus but which showed no

TABLE 1.—*Statistical Analysis of the Mean Permeability Quotients of Poliomyelitic and Control Monkeys*

History of Monkeys	Number of Animals	Mean Permeability Quotient	Standard Deviation	Standard Deviation of Mean
Normal	19	1.76 ± 0.03	0.1819	0.0417
Traumatized controls*				
Starch	5	1.21 ± 0.024	0.080	0.0357
Normal cord	5	1.22 ± 0.026	0.0860	0.0384
Spinal fluid	5	1.23 ± 0.037	0.1276	0.0570
Virus-inoculated				
No symptoms				
Intracerebral route	20	1.15 ± 0.02	0.1068	0.0238
Other routes	9	1.21 ± 0.032	0.1438	0.0479
Typical symptoms				
Nasal inoculation				
Preparalytic	3	1.00 ± 0.013	0.0331	0.0191
Paralytic	4	0.96 ± 0.028	0.1711	0.0428
Cerebral inoculation				
Preparalytic	22	0.99 ± 0.010	0.0707	0.0150
Paralytic	23	0.99 ± 0.009	0.0671	0.0139
Convalescents	12	1.86 ± 0.0438	0.226	0.065

* Received intracerebrally 1 cc. of either a 1 per cent suspension of normal monkey cord, 2 per cent solution of starch or normal monkey spinal fluid.

definite symptoms of infection at any time were higher: for 20 animals receiving virus intracerebrally the mean value was 1.15, while for 9 receiving virus by other routes (intradermally, intravenously) the mean value was 1.21.

Although the quotients of intranasally and of intracerebrally infected monkeys were the same, which indicated that infection and not trauma was responsible for the increase in the permeability of the barrier we deemed it advisable to investigate the effect of cerebral trauma on permeability. To this end 15 normal monkeys were divided into 3 groups of 5 each and were given intracerebral injections of 1 cc. of one of the following agents: a 2 per cent solution of starch, a 1 per cent suspension of normal monkey cord or normal monkey cerebrospinal fluid. The permeability quotients were determined on the fifth to seventh day after the cerebral inoculation. For the group receiving starch

the mean permeability quotient was 1.21, for the group given normal monkey cord it was 1.22, and for group given spinal fluid it was 1.23. These values, while definitely higher than those for monkeys passing through an acute attack of poliomyelitis, were somewhat below those for normal, uninoculated monkeys; the mean quotient determined for 19 normal, unused monkeys was found to be 1.76.

The highest quotients (lowest permeability) were obtained in monkeys convalescent from poliomyelitis. These animals had passed through a typical attack of poliomyelitis three or more months before the bromide test, and all had more or less marked residual paralyses. The mean permeability quotient for this group (12 animals) was 1.86.

Since sodium bromide persists in the body fluids for some time after administration tests of permeability were not done on the same animal in the preparalytic and paralytic stages of the disease. Chart 2 shows

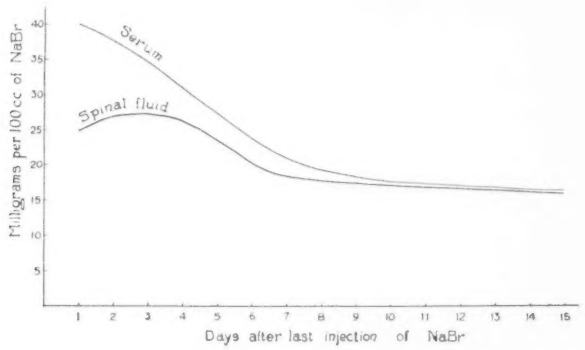

Chart 2.—Rate of disappearance of sodium bromide from the serum and the spinal fluid of normal monkeys.

the rate at which the concentration of sodium bromide changes in the serum and in the spinal fluid after administration by our method. The graphs are based on data derived from 6 normal monkeys. The bromide concentration in the serum decreased rather rapidly for the first six days following the last injection; this period was followed by one in which the rate of loss was much slower. The spinal fluid, on the other hand, usually showed an increase in the bromide concentration for the first three or four days; this was followed by a rapid decrease to a value approximating that found in the serum. Sodium bromide was still detectable in blood and in spinal fluid fifteen days after the last injection, at which time the determinations were discontinued.

Although differences between the mean permeability quotients shown in table 1 appeared to be considerable in some cases, it was thought advisable to evaluate these data by the usual statistical methods. In the present analysis the difference between a given pair of means was

divided by the standard deviation of the difference to obtain the value t. The probability that a difference as great as or greater than that observed will occur by chance alone may readily be calculated from tabled data on the normal curve. The probabilities are shown in table 2. When t becomes greater than 3.86, the probability that the difference between the means is due to chance becomes less than 0.0001. These probabilities have not been calculated, but they are entered in table 2 as significant (S), which indicates that the observed difference between the two means is statistically significant. For example, the probability that the observed difference between the mean permeability quotient for nor-

TABLE 2.—*Probability That the Difference Between Any Pair of Mean Values is Due to Chance Only*

	Control Monkeys for Trauma of Cerebral Inoculation*			Virus-Inoculated Monkeys						
				No Symptoms		Typical Symptoms				
				Intracerebral Inoculation	Other Routes of Inoculation†	Intranasal		Intracerebral		
History of Monkeys	Starch	Normal Cord	Spinal Fluid			Preparalytic	Paralytic	Preparalytic	Paralytic	Convalescent Monkeys
Normal	S‡	S	S	S	S	S	S	S	S	0.19
Traumatized control*										
Starch	....	0.95	0.76	0.16	1.00	S	S	S	S	S
Normal cord	....	....	0.89	0.12	0.87	S	S	S	S	S
Spinal fluid	....	....	....	0.19	0.78	S	S	S	S	S
Virus-inoculated										
No symptoms										
Intracerebral route	....	....	....	....	0.26	S	S	S	S	S
Other routes†	....	....	....	....	....	S	S	S	S	S
Typical symptoms										
Nasal inoculation										
Preparalytic	....	....	....	....	....	....	0.40	0.71	0.80	S
Paralytic	....	....	....	....	....	....	....	0.60	0.45	S
Cerebral inoculation										
Preparalytic	....	....	....	....	....	....	....	....	0.88	S
Paralytic	....	....	....	....	....	....	....	....	....	S

* Received intracerebrally 1 cc. of either a 1 per cent suspension of normal monkey cord, a 2 per cent solution of starch or normal monkey spinal fluid.
† Intradermal and intravenous.
‡ Significant difference with probability of less than 1 in 10,000.

mal, unused monkeys and that of any other group, except the convalescents, was due entirely to chance is less than 0.0001, or 1 in 10,000. On the other hand, when normal monkeys are compared with convalescents the probability of the difference being due to chance is 0.19, or roughly 1 in 5, which is not considered significant.

Table 2 shows that there was no difference between the 3 groups of animals receiving starch, normal cord and spinal fluid intracerebrally. This group of traumatized control animals, it may be noted, gave values which are essentially the same statistically as those obtained for animals which were inoculated with virus (by the intracerebral, intradermal or intravenous route) but did not become infected. Although the permeability quotients for the traumatized control group and for the inoculated symptom-free group tend to approximate those obtained

for poliomyelitic animals, the probability of their coinciding is small enough (1 in 10,000 or less) to be considered negative.

Monkeys in the acute stages of poliomyelitis gave permeability quotients which were statistically the same, regardless of whether the determination was made in the preparalytic or in the paralytic stage or after intranasal or intracerebral inoculation of virus.

COMMENT

From the permeability quotients obtained, it is evident that normal, uninoculated monkeys and monkeys recovered from an attack of experimental poliomyelitis can be classed together; the degree of the permeability of the barrier to bromide in this group was small as compared with that of other groups to be mentioned.

The next large group of animals consisted of those receiving virus or other material intracerebrally, as well as of those receiving virus by routes other than the neural. In this group the permeability of the barrier was considerably increased by the trauma attendant on intracerebral inoculation, as might be expected, but the increase was not quite so large as in those animals definitely passing through an attack of poliomyelitis. In the poliomyelitic group, it will be noted, there was no statistical difference in the permeability quotients, regardless of whether the highly traumatic intracerebral route of inoculation or the more natural intranasal route was used; nor was there any difference in the quotients obtained during either the preparalytic or the paralytic stage of the disease. Infection and not trauma, therefore, was the important element leading to an increased permeability of the barrier.

The significance of an increased permeability in cases of poliomyelitis is difficult to assess. The high quotients (low permeability of the barrier) obtained for normal and for convalescent monkeys were due to relatively large amounts of bromide in the blood serum as compared with that in the cerebrospinal fluid. In the poliomyelitic animals the low quotients (high permeability of the barrier) resulted from the fact that the bromide concentration in the spinal fluid equaled or slightly exceeded that of the serum; as compared with normal or convalescent monkeys, the acutely infected animals had less bromide in the serum and more in the spinal fluid. Chart 2 gives the curves for bromide concentration in the serum and in the spinal fluid of normal monkeys. Theoretically, a low permeability quotient could result from (*a*) an increase in the concentration of bromide in the spinal fluid without any change in the amount of bromide in the serum; (*b*) a decrease in the amount of serum bromide with no change in the spinal fluid bromide, or (*c*) a decrease in serum bromide with a corresponding increase in spinal fluid bromide. The last was found to be the case in poliomyelitis-infected

monkeys. As infected monkeys differed from the controls in having less bromide in the serum and much more in the spinal fluid, one may assume that the low serum bromide resulted from passage of sodium bromide into the spinal fluid, i. e., the permeability of the barrier to sodium bromide was increased in cases of poliomyelitis. Were the bromide concentration in the spinal fluid of infected animals the same as in normal animals, the low permeability quotient resulting from a lesser concentration of bromide in the serum, it would be necessary to rule out a more rapid excretion of bromide from the body in poliomyelitic monkeys.

While our data indicate that sodium bromide passes into the spinal fluid in infected animals with greater facility than in normal animals, they give no indication as to where this passage takes place. A clinical meningeal stage has been described in poliomyelitis, and while meningeal disorders are known to increase permeability of the barrier, there is no evidence that increased permeability here is necessarily due to such a cause. What role the cerebral capillaries, the choroid plexus, the ependymal and glial cells and other elements of the cerebrospinal nervous system may play in increasing the permeability of the blood-CNS barrier has yet to be determined.

SUMMARY AND CONCLUSIONS

The permeability of the blood-CNS barrier to sodium bromide was studied in 127 rhesus monkeys.

Nineteen normal monkeys and 12 convalescent from poliomyelitis gave a permeability quotient approximating 1.8 (low permeability of the barrier).

The permeability quotient for 15 cerebrally traumatized controls and 29 monkeys which were inoculated with virus but showed no symptoms tended to approximate 1.2.

A third group, consisting of 52 poliomyelitic monkeys, gave a permeability quotient of about 1 (high permeability).

There was no statistical difference in the permeability quotients of monkeys in either the preparalytic or the paralytic stage of poliomyelitis, nor was there any difference between nasally and cerebrally inoculated animals.

Our results indicate that experimental poliomyelitis produces an increased permeability of the blood-CNS barrier to sodium bromide.

LEAD POISONING

REPORT OF A CASE, WITH SOME PHYSICOCHEMICAL CONSIDERATIONS

IRVING KOWALOFF, M.D.

BROOKLYN

The application of the principles of physical chemistry to biologic phenomena has elucidated a great many physiologic and pathologic processes and has often led to rational and successful therapy. A noteworthy example of this is the derivation by Henderson from the classic law of mass action of the well known equation which expresses the relation of the bicarbonate and carbonic acid concentration of the blood to the hydrogen ion concentration. In this way was furnished the key to the behavior of the buffers of body fluids under normal and under pathologic conditions. Another illustration is the experimental demonstration that physicochemical laws explain certain phenomena which occur in vitro in a tissue, such as rachitic cartilage, which is bathed in serum containing the slightly soluble salts of calcium, the phosphate and carbonate. Thus the clinical problems of acidosis and alkalosis and certain phases of the complex process of normal and metastatic calcification have been clarified by the application of physical chemistry.

Still another of the many problems of medicine that appear to be yielding to the application of physicochemical principles is that of the treatment of lead poisoning. Influenced by the success of the nutritional chemists in formulating certain laws governing calcium metabolism, Aub attempted to apply analogous principles to the metabolism of lead. After much painstaking work, there appeared in 1925 a report by Aub and his associates [1] in which was presented the theory that the quantity of lead excreted by the body may be varied by disturbing the calcium metabolism. According to these authors, a high calcium intake favored the storage of lead, while a low calcium intake tended to increase the excretion of lead. These conclusions were based on observations dealing with the excretion of lead by animals and by human beings. The authors advocated that during the acute phase of lead poisoning a diet high in calcium in the form of milk and calcium lactate be administered so that the lead would be removed from the circulation and deposited in the

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From the Pediatric Department of the Jewish Hospital.

1. Aub, J. C.; Fairhall, L. T.; Minot, A. S., and Reznikoff, P.: Lead Poisoning, Medicine **4**:1, 1925.

bones. They advised that during the inactive phase the lead be liberated from the bones by the use of a diet low in calcium aided by a substance, such as phosphoric acid or ammonium chloride, which may raise the hydrogen ion concentration of the blood. Aub and his associates explained the relation of calcium metabolism to lead metabolism as follows: Since both lead and calcium may be held in the body at a common site, and since the chemical behavior of some of their salts is similar, the same physiologic conditions should favor the liberation and deposition of both elements. In animals fed with diets low in calcium the bones become rarefied. This abnormal condition is corrected when the calcium in the diet is increased. This means that a low calcium diet will deplete the bones of calcium, whereas a high calcium diet will cause a storage of lime salts in the bones. Since lead behaves like calcium, the deposition of lead in bone should be increased by increasing the calcium intake, and the liberation of lead from bone should be effected by decreasing the calcium intake.

In 1932 Shelling [2] pointed out that such an explanation was not in accord with certain physicochemical principles. That these principles take part in the control of the calcium and the phosphorus level in blood serum was indicated by Howland and Kramer [3] in their studies of the mechanism of calcification and in their attempt to explain its failure in rickets. They pointed out the significance of the principle of the solubility product constant in determining the concentration in the serum of the ions of a slightly soluble salt, such as secondary and tertiary calcium phosphate. By applying this principle, they attempted to explain the reciprocal relation between the concentration of calcium and that of inorganic phosphate in the serum of rats fed on diets deficient in vitamin D and containing varying ratios of calcium to phosphorus. They also explained in this manner the calcium and the inorganic phosphate concentration of the serum of rachitic children fed on diets rich in calcium or rich in phosphorus. In the presence of vitamin D deficiency, an intake of large amounts of calcium and minimal amounts of phosphorus will result in a high calcium concentration of the serum and a low inorganic phosphate concentration. Similarly, a low calcium and a high phosphorus intake will result in a low calcium concentration of the serum and a high inorganic phosphate concentration. If the serum is saturated with calcium phosphate, then the concentration of the ions

2. Shelling, D. H.: Effect of Dietary Calcium and Phosphorus on Toxicity of Lead in the Rat, Proc. Soc. Exper. Biol. & Med. **30**:248, 1932.

3. Howland, J., and Kramer, B.: Factors Concerned in the Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204, 1922. Kramer, B., and Howland, J.: Factors Which Determine the Concentration of Calcium and of Inorganic Phosphorus in the Blood Serum of Rats, J. Nutrition **5**:39, 1932.

of this salt will be governed directly by the principle of the solubility product constant. Such a condition obtains in the presence of adequate intake of vitamin D, as well as of calcium and phosphorus. If the serum is not saturated with calcium phosphate, then the concentration of phosphorus and of calcium in the serum will be regulated by the influence of the principle of the solubility product constant acting in the intestinal canal. Such a condition prevails in active rickets. If an excessively large amount of phosphate is fed, the fecal loss of calcium increases, because more of the insoluble calcium phosphate is formed. The reduction of the amount of soluble calcium in the intestinal fluid leads to a reduction of the calcium in the serum. The excess of phosphorus is absorbed, and a high phosphate concentration of the serum results. If, on the other hand, an undue amount of calcium is fed, the fecal loss of phosphorus increases, because the phosphate in solution is precipitated as calcium phosphate. The excess of calcium is absorbed, which gives rise to a high concentration of the calcium in the serum. The decrease of the soluble phosphate in the intestinal fluid results in a low concentration of phosphate in the serum. Thus, without the stabilizing influence of an adequate intake of vitamin D, the calcium and phosphate concentrations of the blood serum are at the mercy of the changing ratio of these elements in the diet, and the maximum concentration which they may attain is less than when the diet is adequately fortified with vitamin D.

With these facts in mind, Shelling concluded that Aub's therapy was irrational. If the principle of the solubility product constant is valid for the lead phosphate dissolved in the serum, then an abundance of phosphate and foods containing phosphorus should be supplied to raise the phosphate content of the serum in order to precipitate the lead ion from the serum and facilitate its deposition in bone, or its elimination through excretory channels, as the insoluble lead phosphate. But the introduction of large amounts of calcium in the diet, as advocated by Aub, would have the opposite effect, since the intestinal fluid would be depleted of its soluble phosphate by the precipitation of the latter as calcium phosphate. Shelling attributed Aub's success in cases of acute lead poisoning to the fact that he used large quantities of milk, which, besides calcium, contains an abundance of phosphorus.

Shelling presented laboratory evidence for his contention that an abundance of phosphate and foods rich in phosphorus should be supplied in the diet for the treatment of acute plumbism. A number of rats were fed with a certain diet containing a lead salt. Another group received, in addition to lead salt, a calcium salt. A third group received with the lead salt a magnesium salt. All these animals died. However, rats fed with a diet containing a lead salt and disodium phosphate

remained alive, grew and even reproduced. A few animals were fed with a lead salt until they showed evidence of toxicity. Some of these were then fed a diet containing calcium salt and others one containing disodium phosphate. Animals given the phosphate showed marked improvement, while those given the calcium salt did poorly. The rats that had received the phosphate were then given a diet containing an excess of calcium. The toxic symptoms rapidly reappeared, and the animals died in convulsions.

The purpose of this paper is to present clinical and laboratory data in support of the theory that administering a phosphorus-rich diet is the rational treatment of acute lead poisoning. In the pediatric service of Dr. Benjamin Kramer several patients with acute plumbism have been successfully treated with a high phosphorus diet to which phosphate was added in the form of a 10 per cent solution of disodium phosphate. The patients that presented symptoms of lead encephalopathy were first treated with large doses of sedatives to control their convulsions adequately. They were then given a 10 per cent aqueous solution of disodium phosphate, 10 cc. being administered three times a day. The basic diet consisted of a quart (946 cc.) of milk and two eggs daily. To establish the diagnosis of lead poisoning, roentgen study of the long bones was done, the blood smear was carefully examined for stippled red cells, the blood and urine were analyzed for lead and the protein of the spinal fluid was measured. Accessory treatment in the form of a blood transfusion was given if the anemia was severe. A patient was considered to be successfully treated if the clinical symptoms improved and in addition the lead concentration of the blood showed a considerable decrease. One case is reported here in great detail because it was possible to obtain repeated and complete analyses of the blood during the course of treatment. Not only do the results afford evidence of the validity of the principle of the solubility product constant for lead phosphate dissolved in blood serum, but they supply some data which indicate the exact chemical form of the lead salt in the blood. The analyses of the blood involved exact simultaneous chemical determinations of the calcium, phosphorus and lead content.[4] The lead concentration of the whole blood was determined, and the calcium and the phosphorus concentration of the serum.

4. Methods for Determination of the Lead, Calcium and Phosphorus of the Blood: (*a*) Wilkins, E. S., Jr.; Willoughby, E. O., and Smith, F. L., 2nd: Determination of Minute Amounts of Lead in Biological Materials, Indust. & Engin. Chem. (Analyt. Ed.) **7**:33, 1935. (*b*) Kramer, B., and Tisdall, F. F.: A Simple Technique for the Determination of Calcium and Magnesium in Small Amounts of Serum, J. Biol. Chem. **47**:475, 1921. (*c*) Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorus, ibid. **66**:375, 1925.

REPORT OF CASE

M. W., a Negro girl aged 22 months, was admitted to the pediatric service of the Jewish Hospital, with the chief complaint of vomiting of three weeks' duration. The family history revealed that the mother had been treated for syphilis in 1925 and also during her pregnancy. A Kline test of the mother's blood gave a negative reaction. She had had no miscarriages. The Kline test of the father's blood gave a positive reaction. The patient had one brother, aged 5, who was in good health. The girl was delivered spontaneously at term. Her weight at birth was 7 pounds and 6 ounces (3,345 Gm.). The child was well during the neonatal period. Up to the onset of her present illness, her development was normal. Her first tooth appeared at the age of 6 months. She walked at 11 months. She could say only "mammy" and "daddy." At the age of 21 months she weighed 28 pounds (12,700 Gm.). Her diet consisted of milk, eggs and vegetables. She was reported to have received 2 teaspoons (8 cc.) of cod liver oil and 1 ounce (30 cc.) of orange juice daily since the first month. For fifteen months prior to the onset of her illness, the child ate objects from the floor and paint from the window sill. She had daily bowel movements, but the stools were usually hard and small. At the age of 14 months she had pertussis, from which she made an uncomplicated recovery. For three weeks prior to admission to the hospital she vomited frequently during and after meals. She lost 5 pounds (2,268 Gm.). In the last three days before entry she appeared to be ill. She was drowsy and irritable and refused to stand or walk. There were no convulsions.

Physical examination revealed that the patient was well developed but ill, pale and irritable. The temperature, pulse rate and respiratory rate were normal. The blood pressure was 104 systolic and 65 diastolic. The calvarium was normal in size and shape. The fontanels were closed. There was no craniotabes. The gums revealed no lead line. The nose, throat, eyes and ears were normal. The heart was normal, and the lungs were clear. There was no enlargement of the costochondral junctions. Examination of the abdomen revealed nothing abnormal. The extremities presented no rachitic deformities. The lower extremities were so weak that the patient could not stand, but the knee jerks and ankle jerks were active and equal on both sides. There was no muscular spasm or nuchal rigidity. The Kernig sign was absent.

Laboratory examinations revealed the following data: Routine examination of the urine showed nothing abnormal except an occasional white blood cell. Study of the blood showed that the hemoglobin content was 59 per cent; red cells numbered 4,200,000 and white cells 12,600, of which polymorphonuclears constituted 66 per cent, band forms 17 per cent, basophils 1 per cent, lymphocytes 29 per cent and monocytes 3 per cent; the platelets were adequate. A blood smear revealed anisocytosis, increased central pallor and basophilic stippling of the red cells. The reaction to tuberculin was negative. Analysis of the blood serum showed the following values: carbon dioxide–combining power, 44 volumes per cent; chlorides 387 mg., nonprotein nitrogen 29 mg.; total protein 7.9 Gm. and phosphorus 1.2 mg. per hundred cubic centimeters; phosphatase, 8.2 Bodansky units. The lead content of the whole blood was 0.72 mg. per hundred cubic centimeters. Roentgen examination of the long bones revealed a heavy line of condensation at the ends of the diaphysis. The roentgenogram of the skull showed no abnormality. The Kline reaction of the blood was negative.

While this information was being gathered, no special treatment was given. The diet consisted of 3 ounces (89 cc.) of whole milk given every three hours. There were no other articles of food. On the fourth day after admission, the

patient had two convulsions. These were controlled with ether anesthesia and chloral hydrate and sodium bromide given by rectum. A spinal tap at this time revealed 10 cells per cubic millimeter of fluid and 64 mg. of sugar, and 76 mg. of protein per hundred cubic centimeters. The Wassermann reaction of the spinal fluid was negative. The diagnosis was lead encephalopathy. The patient was given daily 30 cc. of a 10 per cent solution of disodium phosphate and a diet consisting of 32 ounces (946 cc.) of whole milk and 2 eggs. As her condition improved, additional articles, consisting of cereal, orange juice, banana and vegetables, were gradually added. The patient also received ½ grain (0.03 Gm.) of phenobarbital every four hours. This was gradually decreased to ¼ grain (0.015 Gm.) given three times a day. With this regimen there was no recurrence of convulsions. However, coarse tremors of the extremities appeared. Two and a half weeks after admission the patient began to stand up in her crib, but she was still unable to walk. One month after entry she began to walk again, but the gait was ataxic. In the meantime, the lead concentration in the blood serum fell steadily. One and a half months after admission, the patient was given two transfusions of citrated blood, each of 150 cc., on consecutive days. After the second transfusion hemoglobinuria appeared, but the temperature rose no higher than 100.4 F. The hemoglobinuria lasted for four days. The patient did not appear to be ill. The blood of the patient and that of the donor were rechecked, and both were found to belong to group B. They were completely compatible with each other. The Kline reaction was negative both for the patient and for the donor. The Donath-Landsteiner test for autohemolysins gave negative reactions for both donor and recipient. Since the second transfusion was given with blood that had been stored in the refrigerator for twenty-four hours, it is possible that certain changes occurred in the red cells of the donor which rendered them more fragile. The hemoglobin content determined one week after transfusion showed a rise from 47 per cent to 69 per cent. The red cell count was 5,100,000. The patient, much improved, was discharged fifty-five days after admission. The tremors of the extremities and the ataxic gait were still present, but they were not as marked as previously. The lead content had diminished from 0.72 to 0.18 mg. per hundred cubic centimeters of the whole blood. The urine showed 0.2 mg. of lead in 440 cc. A spinal tap done just prior to discharge showed only 8 cells per cubic millimeter, and the protein had diminished from 76 to 29 mg. per hundred cubic centimeters. The disodium phosphate therapy was continued at home. Two weeks after discharge the patient was seen again in the outpatient pediatric department. The tremors and ataxia had disappeared, and the weight of the patient had increased.

COMMENT

What evidence is there for attributing this improvement to the high phosphorus diet? The milk with which the patient was fed contained, besides phosphorus, a considerable amount of calcium. However, if it could be demonstrated that a reciprocal relation existed between the phosphate and the lead concentration of the blood of the patient, it would be reasonable to conclude that a high lead concentration depresses the phosphate content and, conversely, that a high phosphate concentration depresses the lead content. In this case such a demonstration should be possible, since there was a series of simultaneous determinations of the calcium, phosphorus and lead concentrations of the blood.

On multiplying the lead and the inorganic phosphorus concentrations, expressed as milligrams per hundred cubic centimeters, I found that the products that I obtained were reasonably constant, since they were all situated in the narrow range between 0.864 and 0.792 points. The inverse relation between the lead and the phosphorus concentration was therefore exact. The data and calculations have been summarized in table 1. Analysis of these figures reveals that at the end of treatment the decrease of lead was 75 per cent, the increase of phosphorus 266 per cent, the decrease of the lead-phosphorus product 8 per cent and the increase of calcium 11 per cent.

It may possibly be pointed out that the presence of 1.2 mg. of inorganic phosphorus per hundred cubic centimeters of blood on the first determination was evidence of rickets. It may then be argued that as the rickets healed large amounts of calcium phosphate were deposited in the bones and that lead phosphate was deposited along with the lime salt. This would confirm Aub's contention that the same physiologic

TABLE 1.—*Calcium, Phosphorus and Lead Content of the Blood of M. W.*

Date	Calcium, Mg. per 100 Cc. of Serum	Phosphorus, Mg. per 100 Cc. of Serum	Lead, Mg. per 100 Cc. of Whole Blood	Lead × Phosphorus
8/ 1/36	...	1.2	0.72	0.864
8/ 6/36	9.3	3.1	.....	.....
8/10/36	9.0	3.2	.....	.....
8/13/36	...	3.2	0.27	0.864
8/28/36	10.3	3.7	0.22	0.814
9/10/36	10.3	4.4	0.18	0.792

conditions favor the liberation and the retention of both calcium and lead. However, there was neither clinical nor roentgen evidence of rickets. The presence of a lead line and the absence of the findings characteristic of rickets can be readily seen in the roentgenogram of the patient's long bones. Moreover, the patient was said to have been given 2 teaspoonfuls of cod liver oil daily since the age of 1 month and to have been fed a diet which included eggs up to the onset of her illness. Apart from the vitamin D content of the milk and eggs, the patient received no intensive vitamin D therapy while in the hospital. If she had had rickets, it would have been remarkable, indeed, for such a low vitamin D intake to have caused the serum phosphorus to rise in five days from 1.2 to 3.1 mg. per hundred cubic centimeters. Finally, the phosphatase of the specimen of blood which contained the extremely low amount of phosphorus was 8.2 units, which is within the limits of normal. Since evidence of rickets was lacking, and since an exact inverse relation between the lead and the phosphorus concentration of the blood was demonstrated, the original low inorganic phosphorus content of the blood was presumably due to the associated high concentration of lead.

The lead-phosphorus product constant of the blood makes one suspect that the solubility product constant of one of the lead phosphate salts may be an important factor in determining the lead and the phosphate concentration of the blood. Aub presented convincing evidence that the salt in the blood is lead phosphate, in part dissolved in the serum and in part held in the solid state by the red cells. Whether lead transported

Roentgenograms of the long bones of M. W.; lead lines and absence of the findings characteristic of rickets can be seen. *A*, forearm; *B*, lower part of leg.

in the blood is in the form of dilead phosphate, $PbHPO_4$, or trilead phosphate, $Pb_3(PO_4)_2$, is difficult to establish, since the amount of lead salt in the blood is so minute that isolation and identification of it is hardly possible. If the lead is assumed to be in the form of the tertiary phosphate, the amount of lead phosphate dissolved in the serum is much greater than would be dissolved in water at the same temperature. Aub therefore offered the theory that the tertiary lead phosphate is carried

in a colloidal state in the blood serum. Such a hypothesis, however, is unnecessary if one assumes that the phosphate has the formula of the secondary lead phosphate, $PbHPO_4$. For, according to Aub and his associates, the dilead phosphate is almost one hundred times more soluble in water than the trilead phosphate.

The chemical data in the present case give some evidence in support of the theory that the lead phosphate dissolved in the serum is in the form of the dilead phosphate. From further calculations, I found that the lead-phosphorus product constant of the blood can be best explained on the assumption that the serum is a saturated solution with respect to dilead phosphate; that the lead carried by the red blood cells is in the solid phase of dilead phosphate; that the Pb and HPO_4 ions in the serum are in equilibrium with the $PbHPO_4$ carried in the red cells, and that the proportion of lead per hundred cubic centimeters of serum to lead per hundred cubic centimeters of whole blood is a constant. If such a theory is correct, one should be able to predict the solubility product constant of $PbHPO_4$. In the following discussion I have assumed that $PbHPO_4$ in solution is completely ionized. This assumption is in accordance with the generally accepted theory of physical chemistry that strong electrolytes, such as salts, are completely dissociated but that the ions are prevented by various influences from exerting their full effect on osmotic pressure and on electrical conductivity. This impeded effectiveness of the ions is known as their reduced activity; it is denoted by a fraction called the activity coefficient.

In calculating the solubility product constant of $PbHPO_4$, the values of Pb and HPO_4 must be expressed in terms of molar concentration, that is, as the number of mols per liter of solution. Since the determination of lead for whole blood measures the solid as well as the dissolved lead salt, an invariant factor must be found which will convert the lead concentration for whole blood into the lead concentration for serum. This involves the assumption that the proportion of lead concentration in serum to that of lead in whole blood is a constant. Blumberg and Scott [5] found on analyzing by the spectrographic method the blood of patients with clinical lead poisoning that about nine tenths of the lead is contained in the red cells and only one tenth in the serum. The volume of normal whole blood is approximately twice that of serum. Since the red cell count of the patient on admission was only slightly below the normal for females, I shall assume that the volume of the patient's serum was about half of that of the entire blood. In order, then, to convert the number of milligrams of lead per hundred cubic centimeters of whole blood to the number of milligrams of lead per

5. Blumberg, H., and Scott, J. F. M.: The Plasma-Cell Partition of Blood Lead in Clinical Lead Poisoning, Bull. Johns Hopkins Hosp. **56**:31, 1935.

hundred cubic centimeters of serum, one must multiply by the factor 0.1×2, or 0.2. The molar concentration of the lead in the serum is then determined in accordance with this formula:

$$[Pb] = \frac{\text{mg. Pb per 1,000 cc. serum}}{\text{atomic weight of Pb}} \times 10^{-3} = \text{mols Pb per 1,000 cc.}$$

In determining the molar concentration of HPO_4,[6] the following facts must be considered. The total inorganic phosphate of the blood is in the form of BH_2PO_4, B_2HPO_4 and B_3PO_4, in which B = Na or K. The tertiary phosphate is only about $\frac{1}{100,000}$ of the total, which is chiefly in the form of the primary and secondary phosphates. The proportions of BH_2PO_4 and B_2HPO_4 depend on the p_H of the serum. They can be determined from the Henderson-Hasselbalch equation for salts of weak acids:

$$p_H = pK^1 + \log \frac{B_2HPO_4}{BH_2PO_4}$$

At p_H of 7.4 the ratio of B_2HPO_4 to BH_2PO_4 is found to be 4:1.

TABLE 2.—*Calculation of Solubility Product Constant (Ksp) of $PbHPO_4$ from Lead and Phosphorus Content of Blood*

	Lead			Phosphorus			
	Mg. Pb in 100 Cc. of Blood	Mg. Pb in 100 Cc. of Serum	Mols of Pb in 1 Liter of Serum [Pb]	Mg. P (total) in 100 Cc. of Serum	Mg. P $(HPO_4)^{--}$ in 100 Cc. of Serum	Mols of HPO_4 in 1 Liter of Serum $[HPO_4]^{--}$	[Pb] × $[HPO_4]$ = Ksp $PbHPO_4$
A	0.72	0.144	6.95×10^{-6}	1.2	0.96	3.10×10^{-4}	2.15×10^{-9}
B	0.27	0.054	2.60×10^{-6}	3.2	2.56	8.26×10^{-4}	2.15×10^{-9}
C	0.22	0.044	2.12×10^{-6}	3.7	2.96	9.55×10^{-4}	2.02×10^{-9}
D	0.18	0.036	1.73×10^{-6}	4.4	3.52	11.4×10^{-4}	1.97×10^{-9}
						Average =	2.07×10^{-9}

B_2HPO_4 is therefore eight tenths of the total inorganic phosphate. The amount of P that is HPO_4 can therefore be determined from the total number of milligrams of phosphorus per hundred cubic centimeters by multiplying by the factor 0.8. The molar concentration of HPO_4 can then be determined from the formula:

$$[HPO_4] = \frac{\text{mg. P (in } HPO_4\text{) per 1,000 cc. serum}}{\text{atomic weight of P}} \times 10^{-3} = \text{mols P or } HPO_4 \text{ per 1,000 cc.}$$

By multiplying the molar concentration of Pb by that of HPO_4 one obtains the solubility product constant of $PbHPO_4$. The results are in the narrow range between 2.15×10^{-9} and 1.97×10^{-9}. The average is 2.07×10^{-9}. These calculations have been summarized in table 2.

How does this compare with the solubility product constant (Ksp) of $PbHPO_4$ as determined from experimental data? According to Aub, the solubility of $PbHPO_4$ in water at 25 C. is 12.9×10^{-3} Gm. per liter. In the following calculations it is assumed that the $PbHPO_4$ is

6. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1.

completely ionized. The mols of Pb and of HPO_4 will therefore each be equal to the mols of $PbHPO_4$.

$$\text{Hence, } [Pb] = \frac{\text{Gm. } PbHPO_4 \text{ in 1,000 cc.}}{\text{molecular weight of } PbHPO_4} = \frac{12.9 \times 10^{-3} \text{ Gm. per 1,000 cc.}}{303.2}$$

$$= 4.2 \times 10^{-5} \text{ mols per liter}$$

and $[HPO_4] = 4.2 \times 10^{-5}$ mols per liter

$[Pb]\ [HPO_4] = \text{Ksp of } PbHPO_4$

$[4.2 \times 10^{-5}]^2 = 1.76 \times 10^{-9} = \text{Ksp of } PbHPO_4$

This agrees closely, of course, with the value obtained from the determinations on the blood, namely, 2.07×10^{-9}.

Since there is good evidence that the principle of the solubility product constant is valid for the lead phosphate of the blood, a high phosphorus diet would appear to be the most rational method of decreasing the lead in the blood.

SUMMARY

A case of lead encephalopathy is presented in which improvement was produced by adequate sedation and a diet high in phosphorus to which 30 cc. of a 10 per cent solution of disodium phosphate was added daily.

Evidence is presented to show that in this case the lead concentration of the blood was determined by the lead-phosphorus product constant of the blood. This constant, expressed in the simplest form, is the product of the lead concentration in milligrams per hundred cubic centimeters of whole blood and the inorganic phosphorus concentration in milligrams per hundred cubic centimeters of serum.

In order to determine the chemical significance of this lead-phosphorus product constant, I made the following assumptions: (1) that the serum is a saturated solution of completely ionized dilead phosphate, $PbHPO_4$; (2) that the lead carried by the red blood corpuscles is in the solid phase of $PbHPO_4$, and (3) that the Pb and HPO_4 ions in the serum are in equilibrium with the solid $PbHPO_4$ of the red cells. I also assumed that the proportion of lead per hundred cubic centimeters of serum to lead per hundred cubic centimeters of whole blood is a constant. With this hypothesis, it was possible to show that the solubility product constant of $PbHPO_4$ determines the lead and the phosphate concentration of the serum. Work is now in progress to test this hypothesis further.

The actual value of this constant, as obtained from my analytic data, is of the same magnitude as that obtained from the value of the solubility of secondary lead phosphate in water, as reported by Aub and his associates.

Since there is good evidence that the principle of the solubility product constant is valid for the lead phosphate of the blood, a diet high in phosphorus (producing a high content of inorganic phosphorus in the serum) would appear to be the most rational method of decreasing the lead concentration of the blood.

MAKING A CORRECTIVE SHOE

LEE BIVINGS, M.D.
ATLANTA, GA.

It has been increasingly apparent to me, after five years' study of weakness in the feet of small children, that two fundamental conditions are present: (1) a rolling in of the ankle, or pronation, and (2) a turning outward of the front part of the foot on the heel, or abduction, which is associated with and possibly a result of the pronation. It would follow, then, that the correction of abnormal position should be the primary purpose of a corrective shoe. It should bring about and maintain the corrected position of supination and adduction, allowing nature in the process of growth, assisted by proper foot balance, to tighten up sagging muscles and ligaments, the result being a normal pair of feet.

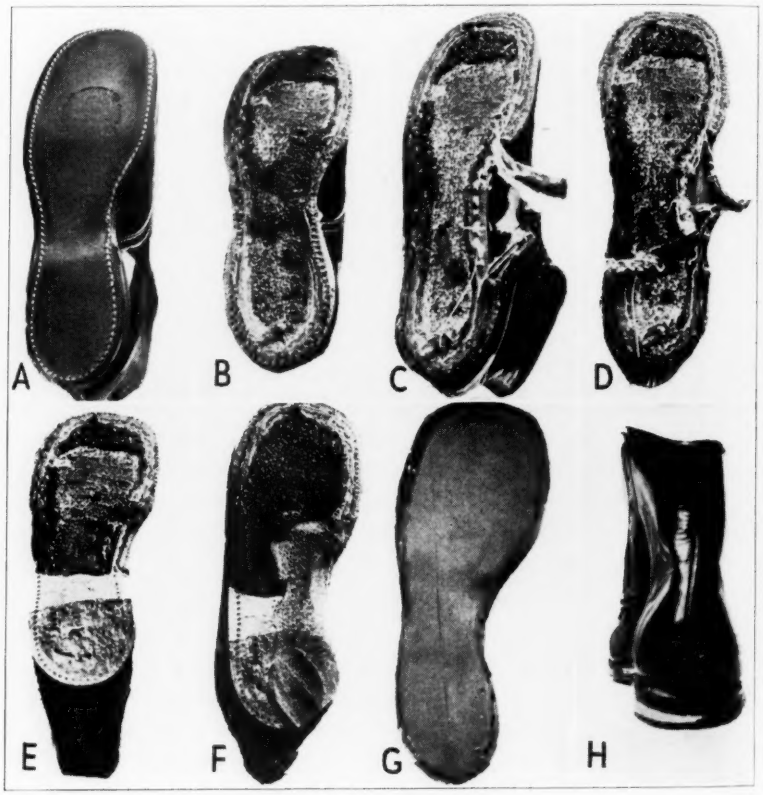
Exercise with proper supervision would greatly help, but with the child in care of the average mother it is either never or improperly done.

There are several excellent corrective shoes on the market at present, but in the smaller communities they are seldom carried in stock. Thus it would seem of value to explain and illustrate a method of making a corrective shoe of any well built, properly shaped shoe designed for a normal foot. One should avoid patent leather because of its tendency to crack and white shoes because they inevitably soften with the persistent application of shoe polish.

It would seem that the prerequisites of a good shoe for the weight-bearing foot should be (1) enough weight to maintain the foot in the normal position of adduction and supination, which demands a stiff sole; (2) a narrow, snugly fitting heel braced by a heavy counter; (3) a swung-in last with the front part broad, and (4) a Goodyear welt process. A midline drawn through the central longitudinal axis of the heel should come out in the region of the fourth or fifth toe, which means that the outer border of the shoe should be almost a straight line, the inner border swinging inward to allow for the adducted position of the front part of the foot.

In the accompanying illustration, *A* shows the sole of such a shoe. In *B*, the sole is cut away from the counter. In *C*, the beading along the inner edge under the arch is cut away and the seam of the upper is cut to allow for overlapping when the swung-in sole is placed on the corrected shoe. In *D*, a wedge is cut out of the insole at the junction of the heel and the instep to allow for the swinging of the sole. In *E*, the overlapping edges of the upper are sewn so as to cause as little wrinkling

as possible. The insole of the shoe is swung in, and the cut edges are sewn together. New beading is put in and sewn in place. The heel is replaced and tapered to fit the swung-in sole better. In *F*, a wedge of the desired thickness, usually from ⅛ to ⅜ inch (0.32 to 0.96 cm.) at the inner border, is placed under the heel; it need not extend beyond the heel, as it does in the photograph. In *G*, the swung-in sole is sewed on. *H* shows the supination accomplished by the wedge.



Stages in the process of making a corrective shoe.

COMMENT

The corrected shoe just described has been found satisfactory for all except extremely weak feet. An unusually weak foot tends to bridge across the swung portion of a corrective shoe, thus breaking the shoe to such an extent that it loses its corrective value. This tendency can be considerably offset by increasing the height of the wedge.

I believe that the ideal time to institute such corrective measures is when the baby first begins to walk, for correct foot balance seems to be the secret of the development of strong feet and contributes materially to good body posture.

Mr. M. A. Sharp and Mr. E. T. Bailey assisted in working out the idea of the shoe described in the present paper.

20 Fourth Street, Northwest.

ACUTE BULBAR POLIOMYELITIS FOLLOWING RECENT TONSILLECTOMY AND ADENOIDECTOMY

MAXWELL STILLERMAN, M.D.
GREAT NECK, N. Y.
AND
ALFRED E. FISCHER, M.D.
NEW YORK

The occurrence of poliomyelitis following tonsillectomy and adenoidectomy was first mentioned in 1928 by Ayer.[1] He cited 9 cases in which the bulbar type developed soon after the operation. The next year, Aycock and Luther [2] described 16 cases in patients whose tonsils had been removed within one month before an attack of poliomyelitis. The onset in all these cases was confined to a seven to eighteen day period following tonsillectomy. In 9 of the cases the infection was of the bulbar type. Silverman [3] subsequently mentioned 5 cases, in 4 of which there was bulbar involvement.

With these observations in mind, we decided to analyze the series of 686 cases of poliomyelitis in patients who were admitted to the Willard Parker Hospital during 1935,[4] in order to determine whether the removal of the tonsils and adenoids in any way influenced the onset or clinical type of the disease. It was found that tonsillectomy and adenoidectomy had been performed in 10 patients during the month antedating their illness. In 8 of these poliomyelitis began ten to twelve days, and in the other 2 sixteen and twenty-two days respectively, after the operation (table 1). Six of the 10 patients had the bulbar or encephalitic form of the disease.

From the Willard Parker Hospital, Department of Hospitals.

Read at the meeting of the New York Academy of Medicine, Section of Pediatrics, March 10, 1938.

1. Ayer, W. D.: Poliomyelitis, Proc. Internat. Assemb. Inter-State Post-Grad. M. A., North America **29**:319, 1928.

2. Aycock, W. L., and Luther, E. H.: The Occurrence of Poliomyelitis Following Tonsillectomy, New England J. Med. **200**:164 (Jan. 24) 1929.

3. Silverman, A. C.: Acute Poliomyelitis in Syracuse, New York, Am. J. Dis. Child. **41**:829 (April) 1931.

4. Fischer, A. E., and Stillerman, M.: Acute Anterior Poliomyelitis in New York in 1935: A Review of Six Hundred and Eighty-Six Cases, Am. J. Dis. Child. **54**:984 (Nov.) 1937.

In view of the high incidence of bulbar poliomyelitis following recent tonsillectomy in the 1935 outbreak, careful inquiry was made among the 52 patients with poliomyelitis that were admitted to the hospital

TABLE 1.—*Data on Patients with Poliomyelitis Following Tonsillectomy and Adenoidectomy*

Case No.	Name	Sex	Age, Years	Date of Operation	Date of Illness	Interval, Days	Type of Poliomyelitis*	Result
				1935				
1	I. T.	M	6	7/25	8/ 4	10	B.	Recovered
2	D. O.	F	18	8/ 6	8/17	11	B.	Recovered
3	R. G.	F	9	8/ 2	8/18	16	B.	Recovered
4	J. W.	M	6	7/31	8/ 9	10	B., S.	Recovered
5	C. S.	F	11	8/ 1	8/13	12	E., S.	Recovered
6	F. H.	M	2	8/17	8/27	10	E., S.	Recovered
7	M. S.	F	3	7/26	8/ 5	10	Upper S.	Recovered
8	V. G.	M	7	9/ 4	9/26	22	Upper S.	Recovered
9	C. H.	M	6	8/ 1	8/13	12	Nonparalytic	Recovered
10	A. P.	M	16	8/15	8/25	10	Nonparalytic	Recovered
				1937				
11	S. B.	M	2	7/ 8	7/22	14	B.	Died
12	R. S.	M	7	7/31	8/13	14	B.	Died
13	S. M.	M	9	8/15	9/ 5	21	B.	Died

* E., encephalitic; B., bulbar; S., spinal.

TABLE 2.—*Incidence of Poliomyelitis in 1935* *

Previous History	Bulbar	Nonbulbar	Total
No recent tonsillectomy	62 (a)	614 (b)	676
Recent tonsillectomy	6 (c)	4 (d)	10
	68	618	686

* Analysis according to the Chi square test: $\chi^2 = 28.509$, $P < 0.0015$.

TABLE 3.—*Incidence of Poliomyelitis in 1937*

Previous History	Bulbar	Nonbulbar	Total
No recent tonsillectomy	12	37	49
Recent tonsillectomy	3	0	3
	15	37	52

TABLE 4.—*Incidence of Poliomyelitis in 1935 and 1937**

Previous History	Bulbar	Nonbulbar	Total
No recent tonsillectomy	74 (a)	651 (b)	725
Recent tonsillectomy	9 (c)	4 (d)	13
	83	655	738

* Analysis according to the Chi square test: $\chi^2 = 38.86$, $P < 0.0015$.

during the year of 1937. It was found that 3 patients had been tonsillectomized within the month preceding their illness. Operation was performed in 2 of these patients fourteen days and in the third

patient twenty-one days before the onset of the disease. All 3 of these had the bulbar type, and all of them died.

As previously stated, in 6 of the 10 recently tonsillectomized patients in the 1935 series the bulbar or encephalitic type of poliomyelitis developed. This was proportionately much greater than the incidence of bulbar and encephalitic forms in the complete series, 68 of 686 cases, or 10 per cent (table 2). In 1937, 15 of the 52 patients had bulbar symptoms, while in all 3 patients who recently had their tonsils and adenoids removed the bulbar type developed (table 3). Thus there was a disproportionately high percentage of bulbar involvement in the tonsillectomized patients in both the 1935 and the 1937 outbreak [5] (table 4).

REPORT OF CASES OBSERVED IN 1935

BULBAR-ENCEPHALITIC TYPE

CASE 1.—I. T., a 6 year old boy, had his tonsils and adenoids removed on July 25, 1935. On August 4, ten days later, he complained of headache and malaise. During the following two days he became drowsy and complained of stiffness of the neck and back. On admission to the hospital, on August 7, he had a temperature of 101.6 F. and was stuporous. He had rigidity of the neck, dysphagia and facial weakness on the left, was unable to swallow and regurgitated fluids through the nose. The spinal fluid was clear and contained 25 cells per cubic millimeter. The nasal regurgitation and dysphagia subsided with the fever at the end of one week. The facial weakness and nasal voice persisted.

CASE 2.—D. O., an 18 year old girl, manifested bulbar poliomyelitis on Aug. 17, 1935. Eleven days previously her tonsils and adenoids had been removed. On the fifth day of her illness she was admitted to the hospital, extremely drowsy, with facial weakness on the left, a nasal twang and difficulty in swallowing. A lumbar puncture yielded clear fluid with 110 cells per cubic millimeter. The patient improved slowly, and she began to swallow liquids without regurgitation on the seventeenth day of her illness. The facial weakness and nasal voice had not improved when she left the hospital.

CASE 3.—R. G., a 9 year old girl, had her tonsils and adenoids removed on Aug. 2, 1935. Sixteen days later there suddenly developed fever, vomiting, difficulty in swallowing and a nasal voice. When seen on the fourth day of her illness she was acutely ill, with a temperature of 102 F., moderate stiffness of the neck and back, a nasal twang and slight dysphagia. The spinal fluid was clear and had a slight increase in the albumin and the globulin content, with 80 monocytes per cubic millimeter. The fever and the difficulty in swallowing subsided on the sixth day of her illness, but the nasal twang persisted.

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5. In order to determine whether the difference between the incidence of cases of bulbar involvement in the tonsillectomized and nontonsillectomized groups was significant, these figures were analyzed according to the Chi square test (Yule, G. U., and Kendall, M. G.: An Introduction to the Theory of Statistics, London, Charles Griffin & Company, 1937). Because the figures for 1937 were too small, the data for two years were combined. It was found that P was less than 0.0015. This means that the probability that our findings were due to chance is only 15 in 10,000.

The figures for 1935 alone gave approximately the same result.

CASE 4.—J. W., a 6 year old boy, had his tonsils and adenoids removed on July 31, 1935. Ten days later he had a headache, which was followed by weakness of the right leg. He was admitted to the hospital on the seventh day of his illness, with a slight weakness of the right side of the face, flaccid paralysis of the right lower extremity and weakness of the left arm and leg and of the back. The spinal fluid was clear and contained 25 monocytes per cubic millimeter. The facial weakness disappeared the day after admission, but the extensive involvement of the trunk and extremities persisted.

CASE 5.—C. S., an 11 year old girl, had a tonsillectomy and an adenoidectomy on Aug. 1, 1935. Twelve days later she became semicomatose and had marked nuchal and spinal rigidity. The spinal fluid was clear and contained 50 cells per cubic millimeter. Drowsiness and mental sluggishness were present for five days. The stiffness of the neck and back persisted for one week, after which weakness of the spinal muscles became evident. She was able to sit up with support at the time of her discharge from the hospital.

CASE 6.—F. H., a 2 year old boy, had a tonsillectomy and an adenoidectomy on Aug. 17, 1935. He convalesced normally until ten days after the operation, when he became listless and drowsy and had difficulty in walking. On August 28, when admitted to the hospital, he had a temperature of 100.8 F.; he was extremely drowsy and was unable to support his head, sit, stand or move the lower extremities. The spinal fluid was clear and contained 35 lymphocytes per cubic millimeter. The diagnosis was polioencephalitis with paralysis of the muscles of the neck and back and of the lower extremities. The lethargy and fever subsided on the third day, but the paralysis persisted; it was unchanged at the time of his discharge, three weeks later.

SPINAL TYPE

CASE 7.—M. S., a 3 year old girl, had a tonsillectomy and an adenoidectomy on July 26, 1935. Ten days after the operation, on August 5, the child had headache, fever and vomiting. On August 10 the family physician after a spinal puncture diagnosed the child's condition as poliomyelitis and referred her to the hospital. She was afebrile when admitted, on the eighth day of her illness. There was moderate stiffness of the neck and back but no definite paralysis. Lumbar puncture yielded clear fluid with 65 cells per cubic millimeter. A few days later weakness of the extensor muscles of the left arm became evident. The nuchal and dorsal rigidity persisted for nine days, after which it was noted that the child could not sit up without support. The paralysis was still present when she left the hospital, two weeks later.

CASE 8.—V. G., a 9 year old boy, had a tonsillectomy on Sept. 4, 1935. On September 26 he had soreness of the throat and pain in the back of the neck. The following day paralysis of the right upper extremity was noted. Lumbar puncture yielded clear fluid with a slight increase in the albumin and the globulin content and 70 cells per cubic millimeter.

NONPARALYTIC TYPE

CASE 9.—C. H., a 6 year old boy, had a tonsillectomy on Aug. 1, 1935. Twelve days later he became ill with headache, vertigo and fever. He complained of pain in the back, dizziness and inability to walk. On the fifth day of his illness he had moderate nuchal rigidity, and Kernig's sign was present bilaterally. Lumbar puncture yielded clear fluid with 52 cells per cubic millimeter. The boy was afebrile after the first day in the hospital. No paralysis developed.

CASE 10.—A. P., a 16 year old boy, had a tonsillectomy and an adenoidectomy on Aug. 15, 1935. Ten days later he had a headache, photophobia and stiffness of the neck. The spinal fluid was clear and contained 140 cells per cubic millimeter. When he was admitted to the hospital, on the third day of his illness, he had moderate stiffness of the neck and was unable to sit up without support. The examination otherwise gave essentially negative results. No paralysis developed.

REPORT OF CASES OBSERVED IN 1937

BULBAR-ENCEPHALITIC TYPE

CASE 11.—S. B., a 2 year old boy, had his tonsils and adenoids removed on July 8, 1937. Fourteen days later he became irritable and began to vomit. The next day he had difficulty in swallowing. When the child was seen by the physician he was acutely ill, with a temperature of 103 F. The respirations were shallow; the voice had a nasal twang, and he regurgitated fluids through the nose. The temperature gradually rose to 105 F.; the respirations became rapid, jerky and shallow and the pulse rapid and weak. Cyanosis appeared, and in spite of the use of a respirator and oxygen therapy the child died twelve hours after admission to the hospital.

Postmortem Examination.—The autopsy was performed three hours after death by Dr. Vera B. Dolgopol. The general pathologic findings were congestion of the lungs, incipient interstitial pneumonia, enlargement of the thymus, mesenteric lymphadenopathy, toxic degeneration of the kidneys and toxic splenitis. The meninges of the brain and spinal cord were greatly congested.

Microscopic Examination: The olfactory bulbs were normal. Perivascular mononuclear cuffing was observed in the red nucleus and in the gray matter surrounding the aqueduct. Cuffing and perivascular hemorrhages were seen in the white matter of the cerebellum. The medulla showed extensive perivascular cuffing in the floor of the fourth ventricle and in both nuclei ambigui. The spinal cord likewise showed perivascular cuffing throughout the gray matter and some degeneration of the motor cells. There was lymphocytic infiltration of the cerebral meninges as well as extensive infiltration of the meninges of the spinal cord.

The pathologic diagnosis was acute polioencephalomyelitis with extensive involvement of the medulla.

CASE 12.—R. S., a 7 year old boy, had his tonsils and adenoids removed on July 31, 1937. Two weeks later he became feverish, had difficulty in swallowing and regurgitated fluids through the nose. When admitted to the hospital he had a temperature of 105 F., convergent strabismus, a nasal twang and dysphagia. Respirations were shallow and jerky; there was retraction of the upper abdominal muscles with inspiration, indicating diaphragmatic paralysis. The spinal fluid was slightly opalescent and contained 100 cells per cubic millimeter, 95 per cent being monocytes. The child died twelve hours after admission. The diagnosis was bulbospinal poliomyelitis.

Postmortem Examination.—This was limited to the cranial cavity; it was performed nine hours after death. The brain and the veins of the meninges were slightly congested.

Microscopic Examination: Sections through the midbrain showed perivascular mononuclear cuffing in the gray matter around the aqueduct; this extended anteriorly to the ocular motor nuclei. In the medulla perivascular infiltration was present in the floor of the fourth ventricle and in the deeper tissues. A hemorrhage had destroyed the dorsal nucleus of one of the vagus nerves. The cervical portion

of the spinal cord showed perivascular cuffing in the gray matter of the anterior and posterior horns. A hemorrhage in one anterior horn had destroyed all ganglion cells. There was lymphocytic infiltration of the meninges on the anterior aspect of the medulla.

The pathologic diagnosis was acute polioencephalomyelitis with extensive involvement of the medulla and upper part of the cervical portion of the spinal cord.

CASE 13.—S. M., a 7 year old boy, had a tonsillectomy and adenoidectomy on Aug. 15, 1937. Twenty-one days later he had headache, fever and vomiting followed by pain in the abdomen. On the fourth day of his illness he had a temperature of 102.4 F., was acutely ill but rational and had dysphagia. Lumbar puncture yielded fluid containing 120 cells per cubic millimeter. On the sixth day of the child's illness the temperature and pulse rate began to rise, the respirations became rapid, irregular and shallow, large quantities of secretions accumulated rapidly in the throat, and cyanosis appeared. The patient's condition became progressively worse, and he died of bulbar paralysis on September 11.

COMMENT

Acute poliomyelitis can be transmitted experimentally to monkeys in various ways. The disease has been produced most readily by intracerebral injection and intranasal instillation of poliomyelitis virus. Other pathways have also been utilized, but these require either special technic, large amounts of virus or, as has recently been shown, specially adapted strains.[6] Under these circumstances, monkeys have been infected by the intestinal, subcutaneous, intraneural, intracutaneous, intraperitoneal and intravenous routes.[7] Notwithstanding experimental data, the route by which the virus enters the human body has not been definitely determined. Toomey [8] and Harmon [9] stated the belief that the virus travels from the intestinal tract along the sympathetic nerve fibers to the spinal cord. The most commonly accepted theory, however, one based on both epidemiologic [10] and laboratory evidence,[11] is that the virus passes through

6. Trask, J. D., and Paul, J. R.: The Skin Infectivity of Poliomyelitis Virus, Science **87**:45 (Jan. 14) 1938.

7. Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932, p. 80.

8. Toomey, J. A.: Spread of Poliomyelitis Virus from the Gastro-Intestinal Tract, Proc. Soc. Exper. Biol. & Med. **31**:680 (March) 1934.

9. Harmon, P. H.: The Use of Chemicals as Nasal Sprays in the Prophylaxis of Poliomyelitis in Man, J. A. M. A. **109**:1061 (Sept. 25) 1937.

10. Aycock, W. L.: The Epidemiology of Poliomyelitis, Long Island M. J. **22**:579 (Oct.) 1928.

11. Brodie, M., and Elvidge, A. R.: The Portal of Entry and Transmission of the Virus of Poliomyelitis, Science **79**:235 (March 9) 1934. Schultz, E. W. and Gebhardt, L. P.: Olfactory Tract and Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **31**:728 (March) 1934. Lennette, E. H., and Hudson, N. P.: Relation of Olfactory Tracts to Intravenous Route of Infection in Experimental Poliomyelitis, ibid. **32**:1444 (June) 1935.

the nasal mucosa along the olfactory nerves and olfactory bulb to the brain, from which it spreads through the central nervous system. Our case reports suggest that the poliomyelitis virus also can enter the body through the traumatized adenoid and tonsillar tissues.

It is generally accepted that the poliomyelitis virus travels along neuron axis-cylinders [12] in the central nervous system. Pette,[13] Hurst [14] and Germain and Trask [15] have demonstrated that trauma greatly facilitates the passage of virus along nerve trunks. The extirpation of the tonsils and adenoids removes a protective barrier and may provide sufficient trauma to the regional nerves to permit the passage into the central nervous system of virus which otherwise might not have entered. The fact that the nerves from the tonsillar and pharyngeal walls lead to the brain stem could explain the development of bulbar and encephalitic forms of poliomyelitis in 9 of the 13 patients who had operations, provided virus were present in the nasopharynx. A spread of virus from the medulla to the adjacent upper cervical segments likewise could account for the relatively high incidence of paralysis of the upper extremities in our cases. Leake [16] reported 12 instances in which poliomyelitis followed injection of vaccines in the attempt to produce active immunity. In every case in which paralysis developed after inoculation, the level of the spinal cord first affected corresponded to the extremity in which the injection had been made. This indicated that the virus traveled directly in nerve trunks to the spinal cord. Our cases of bulbar and upper spinal poliomyelitis following recent tonsillectomy and adenoidectomy strongly suggest that the virus entered the operative field and traveled along the traumatized nerves and in a similar manner produced paralysis at the same level.

The isolation of poliomyelitis virus from secretions of the human nasopharynx is a difficult and often impossible procedure. The virus has been isolated only fourteen times from patients during the acute stage of the disease [17] and in 2 cases from persons who had definite

12. Fairbrother, R. W., and Hurst, E. W.: The Pathogenesis of, and Propagation of, the Virus in Experimental Poliomyelitis, J. Path. & Bact. **33**:17 (Jan.) 1930.

13. Pette, H.: Experimentelle Studien zur Frage der Wanderung ultravisibler Vira auf dem Nervenwege, Deutsche Ztschr. f. Nervenh. **94**:207, 1926.

14. Hurst, E. W.: The Pathogenesis of Experimental Poliomyelitis: Inoculation into the Sciatic Nerve, J. Path. & Bact. **33**:1133 (Oct.) 1930.

15. Germain, W. J., and Trask, J. D.: Cutaneous Infectivity in Experimental Poliomyelitis, J. Exper. Med. **68**:125 (July) 1938.

16. Leake, J. P.: Poliomyelitis Following Vaccination Against This Disease, J. A. M. A. **105**:2152 (Dec. 28) 1935.

17. Stillerman, M., and Brodie, M.: Virus Isolated from Nasal Washings During Acute Poliomyelitis in New York City in 1935, Proc. Soc. Exper. Biol. & Med. **37**:382 (Nov.) 1937.

contact with a patient but did not contract the disease.[18] The virus was also detected by Kramer [19] in the tonsillar and adenoid tissue which had been removed from a child who, as far as was known, had not been exposed to the disease. Although technical difficulties preclude frequent confirmation of them, these observations demonstrate that the virus may be present in the nose and throat not only of a patient with poliomyelitis but of an apparently healthy person who may or may not have been exposed to the disease.

The fact that in all of our cases poliomyelitis developed between ten and twenty-two days after tonsillectomy implies that the virus entered the body either at the time of or shortly after the operation. Our observations are in accord with those originally reported by Aycock and Luther.[2] Aycock [20] has since stated that he learned recently of 2 cases in which bulbar poliomyelitis developed twenty-one days after tonsillectomy and adenoidectomy and that he had heard of others from time to time. Likewise, Ayer [21] has had 6 additional cases since 1928 which he has not reported. The incubation period of the experimental disease in monkeys is usually from six to ten days but may be longer. Fairbrother [22] has shown that a prolonged incubation period may occur when small amounts of virus are injected, since it takes time for the virus to multiply in the central nervous system. Since the throat does not heal completely for at least ten days after tonsillectomy, it is possible that the virus may also enter the healing tissues. A prolonged incubation period, a late entrance or a small dose of virus could account for the delay in the patients who became ill twenty-one or twenty-two days after the operation.

The possibility that these patients might have been infected by a carrier was considered. However, no known common source of contact was found other than 2 patients who were operated on within six days of one another in the same hospital. Moreover, a different surgeon and assistant operated in each case. It is more likely that the virus was

18. (*a*) Flexner, S.; Clark, P. F., and Fraser, F. R.: Epidemic Poliomyelitis: XIV. Passive Human Carriage of the Virus of Poliomyelitis, J. A. M. A. **60**:201 (Jan. 18) 1913. (*b*) Kling, C., and Pettersson, A.: Keimträger bei Poliomyelitis, Deutsche med. Wchnschr. **40**:320, 1914; abstracted, München. med. Wchnschr. **61**:436, 1914.

19. Kramer, S. D.: Detection of a Healthy Carrier of Virus of Poliomyelitis Without History of Contact, Proc. Soc. Exper. Biol. & Med. **32**:1165 (April) 1935.

20. Aycock, W. L.: Personal communication to the authors.

21. Ayer, W. D.: Personal communication to the authors.

22. Fairbrother, H. W.: Immunization of the Horse with the Virus of Poliomyelitis and the Production of an Antiviral Serum, Brit. J. Exper. Path. **11**:43 (Feb.) 1930.

already present in those patients' throats at the time the tonsillectomy and adenoidectomy were done.

We realize that a certain number of children have their tonsils and adenoids removed every summer. It is impossible to determine how many of these might have contracted poliomyelitis in the normal course of events. At some future time an attempt will be made to estimate the normal incidence of tonsillectomy and adenoidectomy during the summer months in an epidemic area and to determine whether there is a significant increase in the rate of poliomyelitis, especially the bulbar form, in recently tonsillectomized patients. In the cases which we are reporting, the definite time relation between the operation and the onset of poliomyelitis, together with the high percentage of bulboencephalitic types of the disease, strongly indicated a causal relation. We suggest that cases of poliomyelitis which develop within a month of tonsillectomy and adenoidectomy be reported in order that additional data may be obtained as to whether this operation affects the incidence and character of poliomyelitis during an epidemic.[23] However, in view of our findings we believe that it is reasonable to postpone tonsillectomy and adenoidectomy or other nonemergency operations in the area of the nose and throat during an epidemic of poliomyelitis.

SUMMARY AND CONCLUSIONS

Thirteen cases of acute anterior poliomyelitis following tonsillectomy and adenoidectomy are reported.

In these cases the disease occurred from ten to twenty-two days after the operation.

The bulboencephalitic type developed in 9 of the 13 cases.

The interval between the operation and the onset of the disease and the much higher incidence of bulboencephalitic forms suggest the operative field as the portal of entry of the virus into the central nervous system.

Tonsillectomy and adenoidectomy should not be encouraged when poliomyelitis is epidemic.

21 Barstow Road.

73 East Ninetieth Street.

23. Since this paper was submitted several articles have appeared substantiating our findings from an experimental and clinical point of view. Sabin, A. B.: Experimental Poliomyelitis by the Tonsillopharyngeal Route with Special Reference to the Influence of Tonsillectomy on the Development of Bulbar Poliomyelitis, J. A. M. A. **111**:605 (Aug. 13) 1938. Poliomyelitis in Ontario in 1937, report of the Department of Health, Ontario, Canada, March 1938. Eley, R. C., and Flake, C. G.: Acute Anterior Poliomyelitis Following Tonsillectomy and Adenoidectomy with Special Reference to the Bulbar Form, J. Pediat. **13**:63 (July) 1938.

COPPER AND IRON IN HUMAN BLOOD

COMPARISON OF MATERNAL AND FETAL BLOOD AFTER NORMAL DELIVERY AND AFTER CESAREAN SECTION

ADOLPH SACHS, M.D.

VICTOR E. LEVINE, M.D.

WILLIAM O. GRIFFITH, M.D.

AND

CLIFFORD H. HANSEN, M.D.

OMAHA

In a previous publication,[1] some of us reported copper and iron values for maternal and fetal blood in 5 cases in which delivery was spontaneous and normal. It was shown that the maternal blood was in every case very rich in copper and in most cases somewhat low in iron, reflecting the so-called anemia of pregnancy. The fetal values presented in every case a very low content of copper and in all instances except one a high content of iron.

Recently, Horváth and Hollósi [2] published observations which indicate that the polycythemia of the newborn, an almost universally accepted phenomenon, is absent in babies delivered by cesarean section and in those subjected to a minimum of birth trauma. They reported for these infants red cell counts which rarely exceeded 5,000,000 per cubic millimeter of blood. On the basis of this and of other data,[3] they maintained also that there is no polycythemia in the intrauterine life of the fetus, a theory that is not in accord with the general belief that because of the lowered oxygen tension present, a polycythemia does exist in utero. Horváth and Hollósi expressed the belief that the polycythemia of the normally born infant is produced by certain factors which are at work only during labor, when the fetus is passing through the birth canal.

In the present paper, we report a comparative study which we have made of the red cell counts and of the concentrations of iron and copper

From the Department of Medicine, Creighton University School of Medicine.

1. Sachs, A.; Levine, V. E., and Fabian, A. A.: Copper and Iron in Human Blood, Arch. Int. Med. **55**:227 (Feb.) 1935.

2. Horváth, Z., and Hollósi, C.: Birth Pains and the Blood of the Newborn, Am. J. Dis. Child. **49**:689 (March) 1935.

3. Hollósi, C., and Horváth, Z.: Hemoglobin Index and Jaundice of the Newborn, Am. J. Dis. Child. **49**:638 (March) 1935.

in the whole blood of babies born by normal delivery and by cesarean section. If the red cell counts of the two groups differ markedly,[2] we might reasonably expect the iron and copper contents of the blood to show important differences. In this study, the values for the fetal blood are compared also with those for the mother's blood in each case.

METHODS

The determinations of iron and copper reported in this paper were made during the months from November 1935 to September 1936. Special precautions were taken

TABLE 1.—*Comparison of Values for Copper Content and Iron Content of Maternal and Fetal Blood in Cases of Cesarean Section*

			FETAL VALUES Cord Blood				MATERNAL VALUES Venous Blood			
No.	Anesthetic	Sex	Red Cells per Cu.Mm.	Iron, Mg. per Hundred Cc.	Hemoglobin, Gm. per Hundred Cc.	Copper, Mg. per Hundred Cc.	Red Cells per Cu.Mm.	Iron, Mg. per Hundred Cc.	Hemoglobin, Gm. per Hundred Cc.	Copper, Mg. per Hundred Cc.
1	Gas	M	4,480,000	50.73	15.15	0.099	3,282,000	36.63	10.09	0.244
2	Spinal	M	4,640,000	56.07	16.74	0.119	3,670,000	42.08	12.56	0.256*†
3	Gas	F	4,720,000	54.70	16.31	0.109	3,820,000	44.45	13.27	0.212
4	Gas	M	4,800,000	55.35	16.52	0.112	4,140,000	44.56	13.30	0.210
5	Gas	F	4,530,000	51.08	15.25	0.097	4,160,000	42.12	12.59	0.244
6	Spinal	F	4,820,000	53.60	16.00	0.091	.....	28.44	8.49	0.254*‡
7	Gas	M	4,960,000	52.81	15.76	0.115	3,990,000	42.44	12.60	0.219
8	Spinal	M	5,020,000	53.53	15.98	0.102	3,810,000	36.65	10.94	0.244
9	Spinal	F	5,940,000	61.80	18.45	0.122	4,020,000	39.60	11.82	0.196*§
10	Spinal	F	5,160,000	54.63	16.31	0.102	4,110,000	40.08	11.96	0.208
11	Spinal	F	4,880,000	53.94	16.10	0.099	4,280,000	44.16	13.18	0.208
12	Spinal	F	4,830,000	53.11	15.85	0.090	4,060,000	38.94	11.62	0.173
13	Spinal	M	5,160,000	54.78	16.35	0.104	3,660,000	34.54	10.31	0.210
14	Gas	M	5,160,000	57.26	17.09	0.120	3,540,000	30.61	9.14	0.231*‖
15	Gas	M	4,860,000	54.89	16.39	0.101	4,000,000	36.57	10.92	0.162
	Averages*		4,855,000	53.60	16.00	0.103	3,937,000	40.11	11.90	0.212

* The cases marked by an asterisk (*) were excluded in determining the averages.
† Mother had diabetes mellitus.
‡ Mother had nephritis.
§ Fetal values here are for one of twins.
‖ Mother had diabetes mellitus.

to obtain pure reagents, free from copper and iron. Acids, alkalis and water were redistilled from glass and were tested at frequent intervals for contamination.

The determinations of copper were made on 5 cc. samples of whole blood by an iron precipitation modification of the method of McFarlane,[4] using sodium diethyldithiocarbamate. The determinations of iron were made on 5 cc. samples of whole blood by a dry ashing method devised in this laboratory, and the results were checked on 0.5 cc. samples by a modification of Wong's wet ashing procedure. Details of the method for copper [1] and of the two procedures for iron [5] have been described previously.

4. McFarlane, W. E.: Application of Sodium Diethyldithiocarbamate Reaction to Micro-Colorimetric Determination of Copper in Organic Substances, Biochem. J. **26**:1022, 1932.

5. Fabian, A. A.; Sachs, A., and Levine, V. E.: Comparison of Wet and Dry Ashing Methods for Determining Blood Iron, Proc. Soc. Exper. Biol. & Med. **32**: 662, 1935.

Seven cubic centimeters of blood was drawn from the umbilical cord immediately on delivery of the baby, and a like volume was taken at the same time from the cubital vein of the mother. The blood was placed in a wide-mouthed tube containing 0.02 Gm. of copper-free and iron-free sodium oxalate. In most cases the cord blood was drawn before tying or cutting, and in every case this was done while the blood in the umbilical vessels was unclotted and freely flowing. Fetal red cell counts were made on cord blood with certified pipets and counting chambers.

TABLE 2.—*Comparison of Values for Copper Content and Iron Content of Maternal and Fetal Blood in Cases of Normal Delivery*

		FETAL VALUES Cord Blood				MATERNAL VALUES Venous Blood				
No.	Sex	Red Cells per Cu.Mm.	Iron, Mg. per Hundred Cc.	Hemoglobin,* Gm. per Hundred Cc.	Copper, Mg. per Hundred Cc.	Red Cells per Cu.Mm.	Iron, Mg. per Hundred Cc.	Hemoglobin,* Gm. per Hundred Cc.	Copper, Mg. per Hundred Cc.	Comment
1	F	4,850,000	57.63	17.20	0.094	4,250,000	41.22	12.30	0.220	Spontaneous Multipara
2	F	4,860,000	57.08	17.04	0.105	4,020,000	43.81	13.08	0.218	Spontaneous Multipara
3	M	4,780,000	54.31	16.21	0.108	3,320,000	38.96	11.63	0.241	Spontaneous Multipara
4	M	5,130,000	50.10	14.96	0.097	4,430,000	38.23	11.41	0.178	Spontaneous Primipara
5	M	5,050,000	59.88	17.87	0.097	3,940,000	39.27	11.72	0.180	Spontaneous Primipara
6	F	5,120,000	53.60	16.00	0.097	4,580,000	41.96	12.53	0.298	Long labor Primipara
7	M	4,800,000	53.83	16.07	0.101	4,060,000	32.48	9.70	0.230	Short Spontaneous Multipara
8	F	4,820,000	53.46	15.96	0.091	4,370,000	44.66	13.33	0.207	Long labor Primipara
9	F	5,240,000	54.96	16.44	0.109	4,920,000	47.17	14.08	0.184	Spontaneous Primipara
10	F	5,040,000	52.42	15.35	0.101	4,420,000	46.73	13.95	0.177	Long labor Mid forceps Primipara
11	F	4,450,000	50.43	15.05	0.081	3,760,000	40.58	12.11	0.193	Spontaneous Multipara
Averages		4,922,000	54.34	16.21	0.098	4,188,000	41.37	12.35	0.211	

* Hemoglobin calculated from blood iron by the formula: Mg. of iron per hundred cc. ÷ 3.35 = Gm. of hemoglobin per hundred cc.

EXPERIMENTAL DATA

The red cell count and the iron, hemoglobin and copper contents of the whole blood for the mother and for the infant in 15 cases of delivery by cesarean section are included in table 1. Four of the 15 cases were excluded from the averages because there were abnormalities which might have affected those figures.

In table 2, similar maternal and fetal values are included for 11 cases of delivery by the normal pelvic route.

COMMENT

It is evident from a study of the tables that whether the newborn infants have been delivered normally or by cesarean section, the fetal red cell counts, iron and hemoglobin contents are from 20 to 25 per cent higher than the corresponding maternal figures. When compared with the values of 4,500,000 red cells, 43.42 mg. of iron and 12.96 Gm. of hemoglobin, which represent the averages for normal women,[1] the maternal figures are seen to reflect what has been called the physiologic anemia of pregnancy.

The copper content of maternal blood at the time of birth, on the other hand, is more than twice as high as that of fetal blood and from one and a half to two times higher than that of the blood of normal adults. This hypercupremia, which has also been shown to exist during the greater part of pregnancy,[6] is proportionately too great to be considered the usual hypercupremic response for the stimulation of hematopoiesis which is seen in other anemias. In addition, it is to be noted that the hypercupremia occurs even when the iron and hemoglobin contents are normal. As has been suggested,[1] the explanation may lie in the fact that the maternal blood transports copper to the fetus and must therefore maintain an increased amount of this element.

After diffusion of the copper through the placenta, the fetus does not retain most of the element in its blood stream but evidently stores it in the liver. The fetal liver has been found to contain from six to ten times as much copper per kilogram of weight as does the liver of an adult.[7] The fact that the liver and the spleen serve as reservoirs for the greater portion of the copper may be associated with the importance of these organs as centers of hematopoiesis in the embryo.

The high iron content and hemoglobin content in blood drawn from the umbilical cord cannot be explained on the basis of the polycythemia of the newborn, because the red cell counts, at least those on cord blood, show no polycythemia in either normally born or cesarean born infants. The only other explanation seems to be that more iron and hemoglobin is carried by each red cell in the fetus. This means either that each cell carries a more concentrated form of hemoglobin or that the cells in fetal blood are larger than those in the blood of a

6. Gorter, E.; Grendel, F., and Weyers, W. A. M.: Le rôle du cuivre dans l'anémie infantile, Rev. franç. de pédiat. **7**:747, 1931. Locke, A.; Main, E. R., and Robash, D. O.: Copper and Non-Hemoglobinous Iron Contents of Blood Serum in Disease, J. Clin. Investigation **11**:527, 1932. Krebs, H. A.: Ueber das Kupfer im menschlichen Blutserum, Klin. Wchnschr. **7**:584, 1928. Tompsett, S. L., and Anderson, D. F.: Copper in Pregnancy, Brit. J. Exper. Path. **16**:67, 1935. Sachs, Levine and Fabian.[1]

7. Sheldon, J. H., and Ramage, H.: A Spectrographic Analysis of Human Tissues, Biochem. J. **25**:1608, 1931. Cunningham, I. J.: Some Biochemical and Physiological Aspects of Copper in Animal Nutrition, ibid. **25**:1267, 1931.

normal adult. The measurements for the diameter of the fetal cells and determinations of their volume indicate that the red cells in the newborn are actually larger than those in the adult.[8]

A comparison of averages for the normal group and for the cesarean group discloses only very small differences, none of which is significant. The variation in red cells between the two groups is less than 100,000; the iron content varies by less than 1 mg. per hundred cubic centimeters, the hemoglobin by only 0.21 Gm. and the blood copper by only 0.005 mg. These differences are well within the range of experimental or distributory error.

The failure to encounter polycythemia in these cases and the sameness of the blood counts for infants born by cesarean section and those normally delivered is disconcerting. A perusal of the literature appears at first glance only to add to the confusion as regards the presence or absence of polycythemia in the newborn. However, closer scrutiny discloses that the reason for the discrepancy in results lies in the source of the blood from which the counts are made. Those workers who have made red cell counts on capillary blood from the heels or the toes of newborn infants have reported polycythemia without exception. Investigators who have made erythrocyte counts on blood from the umbilical cord have found no polycythemia, the counts being comparable to those for adults and in some instances being even lower than the accepted standards for adults.

Among those using capillary blood as a source for their counts are Forkner,[9] who reported an average count of 5,963,000, Lucas and his associates,[10] with an average of 6,080,000, and Lippman,[11] whose figures showed a highest average of 5,600,000 reached six hours after birth. The studies of Aitken [12] suggested that the polycythemia increases after birth, and his maximum figure of 8,330,000 was reached only after forty-eight hours. Merritt and Davidson [13] reported a mean average count of 5,950,000 for newborn infants on the first day of

8. (*a*) Silvette, H.: Study of Erythrocyte Diameters, J. Lab. & Clin. Med. **13**:245, 1927. (*b*) Wintrobe, M. M., and Shumacker, H. B., Jr.: Erythrocyte Studies in Mammalian Fetus and Newborn, Am. J. Anat. **58**:313, 1936. (*c*) Haden, R. L., and Neff, F. C.: The Volume Index and Color Index of Red Blood Corpuscles in New-Born Infants, Am. J. Dis. Child. **28**:458 (Oct.) 1924.

9. Forkner, C. E.: Studies on Living Blood Cells in the Newborn, Bull. Johns Hopkins Hosp. **45**:75, 1929.

10. Lucas, W. P., and others: Blood Studies in the Newborn, Am. J. Dis. Child. **22**:525 (Dec.) 1921.

11. Lippman, H. S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the Newborn Period, Am. J. Dis. Child. **27**:473 (May) 1924.

12. Aitken, J.: Blood Counts in the Newborn, J. Obst. & Gynaec. Brit. Emp. **1**:414, 1902.

13. Merritt, K. K., and Davidson, L. T.: The Blood During the First Year of Life, Am. J. Dis. Child. **46**:990 (Nov., pt. 1) 1933.

life. Sanford,[14] in one of the largest series reported, found an average count of 5,800,000.

The investigators using blood from the umbilical cord reported much lower results. Mugrage and Andresen[15] established 4,860,000 as the mean average erythrocyte count in their series, and Guest and Brown[16] found an average count of 4,770,000. Wintrobe and Shumacker[17] stated that "in studies made with Eastman and Jack, one of us (Wintrobe) found erythrocyte counts in newborn infants which were slightly lower than the average values for adults."

Horváth and Hollósi[2] compared counts on blood from the umbilical vein with those on capillary blood from the infant's heel in cases both of normal and of cesarean delivery. They found the average red cell count in cases of normal delivery to be 4,500,000 per cubic millimeter for cord blood and 5,420,000 for capillary blood, with the latter reaching a peak of 6,250,000 two hours after birth. Their figures for red cell counts of infants born by cesarean section showed an average of 4,390,000 for cord blood and an identical average of 4,390,000 for capillary blood. The capillary count reached its peak two hours after birth, with an average of 4,990,000. These averages were for infants born by a cesarean section in which there was an expansion of only 1 inch (2.5 cm.) in the maternal uterine orifice, and they represented newborn infants subjected to a minimum of trauma during labor, previous to surgical intervention.

In a group of infants delivered by cesarean section from mothers in whom labor had progressed to a stage of 2 inch (5 cm.) dilatation of the uterine orifice, Horváth and Hollósi reported average red cell counts of 4,300,000 for cord blood and 4,670,000 for capillary blood, with the latter rising to a high average of 5,800,000 at four hours after birth.

We have studied another series of newborn infants comparing cord counts with capillary counts made from the heel. The results are shown in tables 3 and 4. The averages in these tables indicate that in our series, at least, the capillary counts are appreciably higher both for normally born infants and for those delivered by cesarean section, although there is a greater difference between cord and cutaneous blood counts for those born by passage through the birth canal than for those delivered by section.

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14. Sanford, H. M.: The Effect of Ultraviolet Light on the Blood of Newborn Infants, Am. J. Dis. Child. **35**:9 (Jan.) 1921.

15. Mugrage, E. R., and Andresen, M. I.: Values for Red Blood Cells of Average Infants and Childen, Am. J. Dis. Child. **51**:775 (April) 1936.

16. Guest, G. M., and Brown, E. W.: Erythrocytes and Hemoglobin of the Blood in Infancy and in Childhood, Am. J. Dis. Child. **52**:616 (Sept.) 1936.

17. Wintrobe, M. M., and Shumacker, H. B., Jr.: Comparison of Hematopoiesis in Fetus and During Recovery from Pernicious Anemia, J. Clin. Investigation **14**:837, 1935.

TABLE 3.—*Comparison of Cord Blood and of Capillary Blood in Newborn Infants Delivered by Cesarean Section*

No.	Sex	Red Cells per Cu.Mm. (Cord Blood)	Red Cells per Cu.Mm. (Blood from Heel)	Time After Birth When Capillary Count Was Taken
1	F	4,810,000	5,760,000	30 min.
2	F	4,620,000	5,210,000	1 hr.
3	M	5,000,000	5,920,000	4 hr.
4	F	4,450,000	5,790,000	1½ hr.
5	M	4,670,000	5,270,000	1 hr.
6	M	4,860,000	5,420,000	30 min.
7	M	4,720,000	5,260,000	2 hrs.
8	F	4,840,000	5,060,000	1 hr.
Averages.....		4,746,000	5,461,000	

TABLE 4.—*Comparison of Cord Blood and of Capillary Blood in Newborn Infants Delivered by Normal Pelvic Route*

No.	Sex	Red Cells per Cu.Mm. (Cord Blood)	Red Cells per Cu.Mm. (Blood from Heel)	Time After Birth When Capillary Count Was Taken	Comment on Labor
1	F	4,510,000	4,770,000	1 hr.	Multipara Normal
2	F	4,860,000	5,820,000	2 hrs.	Multipara Normal
3	M	4,860,000	4,660,000	4 hrs.	Multipara Easy, normal
4	M	4,500,000	5,820,000	2 hrs.	Primipara Difficult
5	F	4,920,000	5,580,000	1 hr.	Primipara Normal
6	F	4,660,000	6,610,000	2 hrs.	Multipara Induced
7	F	5,030,000	7,070,000	1 hr.	Primipara Normal
8	M	4,970,000	5,330,000	4 hrs.	Primipara Normal
9	F	5,040,000	5,790,000	2 hrs.	Primipara Difficult
10	M	4,850,000	5,930,000	5 hrs.	Primipara Abruptio placentae
11	F	5,210,000	6,080,000	2 hrs.	Primipara Difficult
12	M	4,330,000	6,990,000	1 hr.	Primipara Normal
13	M	4,770,000	5,850,000	4 hrs.	Multipara Easy
14	M	4,050,000	5,230,000	2 hrs.	Primipara True knot in cord
15	M	4,680,000	5,730,000	1 hr.	Primipara Premature 8 mo.
16	F	4,580,000	5,585,000	14 hr.	Multipara Normal
17	F	4,540,000	5,360,000	20 min.	Primipara Normal
18	F	5,090,000	6,220,000	1 hr.	Primipara Normal
19	F	4,750,000	5,610,000	2 hrs.	Multipara Normal
Averages.....		4,747,000	5,791,000		

Several theories have been offered to explain the polycythemia which is reflected in the capillary blood. We have previously mentioned the theory of lowered oxygen tension in utero which simulates the rarefied atmosphere at high altitudes and might well cause compensatory increase in red blood cells.

Aitken,[12] Elder and Hutchison [18] and Frank [19] expressed the theory that the erythraemia neonatorum represents a concentration of the blood due to dehydration in the birth process. Forkner [9] spoke against the concentration theory because curves worked out by him for concentration of blood serum protein did not run parallel with curves representing concentration of red blood corpuscles. Another group, headed by Lippman [11] in recent years, stated the belief that polycythemia is the result of an increased hemopoietic activity of the fetus.

Haden and Neff [8c] showed that for several days after birth cutaneous blood counts of the newborn are much higher than counts made on venous blood from the longitudinal sinus. They decided that the higher count in peripheral blood is related in some way to the increased volume of the individual red cell, a condition which might well cause stagnation of the cells in the capillaries. In pernicious anemia, a fundamental and characteristic change in the blood is the increase in the size of the red cells. Duke [20] pointed out that in this disease the cell counts are often higher in peripheral than in venous blood.

The polycythemia of the newborn has in the past been generally believed to be an absolute rather than a relative polycythemia. The high icteric index of the blood serum of nearly all infants in the first week of life and the clinical jaundice which is visible in many infants were attributed to the increased amount of bile pigment produced by the destruction of the excessive numbers of erythrocytes present at birth. However, in recent years this view has been challenged. Elton [21] expressed the opinion that a patent ductus venosus at birth might well account for icterus neonatorum. He stated: "The period of the patency of the ductus venosus Arantii, which acts as an Eck fistula during the first few days of life, corresponds exactly with the phenomenon of icterus neonatorum."

A functioning ductus venosus diverts the majority of the blood from the portal circulation directly into the vena cava, without passage

18. Elder and Hutchison: Some Observations on Maternal and Fetal Blood at Birth, Edinburgh M. J. **41**:105, 1895.

19. Frank, M.: Beitrag zur Biologie der weissen Blutzellen in der Neugeburtzeit und im Säuglingsalter, Ztschr. f. Kinderh. **31**:16, 1921.

20. Duke, W. W.: Specific Tests in the Diagnosis of Allergy, Arch. Int. Med. **32**:298 (Aug.) 1923.

21. Elton, N. W.: The Van Den Bergh Reaction (Ring Test Technic) and Hemoglobin-Bilirubin Interrelation in Icterus Neonatorum, J. Lab. & Clin. Med. **20**:817, 1935.

through the liver sinusoids, and greatly impairs the efficiency of the liver as an excretory organ for bilirubin. As a result, retention of excess bile pigment in the blood stream and consequent jaundice may result even in the presence of a normal rate of red cell destruction.

It is also conceivable, as Snelling [22] and Rich [23] pointed out, that the endothelial cells of the liver, which have previously been engaged in hemopoietic activity, cannot at birth immediately assume the role of removing the bilirubin from the blood stream and transmitting it to the periportal lymph spaces, where it is to be excreted by the liver cells.

It becomes apparent, therefore, that while an increased bilirubin content and an increased icteric index in the blood of newborn infants is to some extent dependent on increased destruction of red cells, there are other factors controlling the degree of bilirubinemia which are not hematogenous. Consequently, a high icteric index is in itself not to be taken as proof of polycythaemia neonatorum.

It seems possible also that shock due to manipulation and trauma in the birth process or surgical trauma in cesarean section might well account for an increase in the capillary counts, if one accepts the present day explanation of shock offered by many physiologists. Krogh,[24] of Denmark, and Lewis,[25] of Great Britain, made extensive studies on the physiology of the capillaries, and their results agreed in showing that the cause of shock is loss of capillary tonus and dilatation and increased permeability of the capillary walls. This combination of factors allows for loss of blood plasma and produces a concentration of blood in the capillaries accompanied by a decrease in total blood volume.[26] As a result of the concentration of corpuscles in the capillary tree, Cannon and his associates [27] conclusively demonstrated, blood taken from surface capillaries, such as the lobe of the ear or the finger or toe, in shock shows red cell counts which exceed by as much as 2,000,000 per cubic millimeter counts on venous blood taken from the same person at the same time. Even in moderate degrees of shock, these

22. Snelling, C. E.: Icterus Neonatorum, J. Pediat. **2**:399, 1933.

23. Rich, A. R.: Pathogenesis of Form of Jaundice, Bull. Johns Hopkins Hosp. **47**:338, 1930.

24. Krogh, A.: Anatomy and Physiology of the Capillaries, ed. 2, New Haven, Conn., Yale University Press, 1929.

25. Lewis, T.: Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

26. Keith, N. M., in Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions: VIII. Traumatic Toxemia as a Factor in Shock, Medical Research Committee, Special Report Series, no. 26, London, His Majesty's Stationery Office, 1919, p. 36.

27. Cannon, W. B.; Fraser, J., and Hooper, A. N.: Some Alterations in Distribution and Character of Blood in Shock and Hemorrhage, J. A. M. A. **70**:526 (Feb. 23) 1918.

workers found that capillary counts exceeded counts made on venous blood by 1,000,000 in many cases. Their results were corroborated by Robertson and Bock.[28]

In the capillary region, the corpuscles are exposed the most to contact with the vascular wall; that is, in this region friction is greatest, and the energy stored in the arterial pressure is largely used up. When arterial pressure is low, as in shock, there is naturally a tendency for the blood corpuscles to gather in the place of greatest resistance, namely, the capillaries.[29] Suggs[30] stated that nearly all babies suffer some degree of shock as a result of birth trauma.

Whatever the explanation may be, the fact remains that polycythemia exists in the capillary blood of the newborn but not in blood taken from the umbilical cord.

SUMMARY

Red cell counts made on blood from the umbilical cord of newborn infants delivered by cesarean section are compared with similar values for normally born infants. No appreciable difference is shown.

Red cell counts taken from the heels of newborn infants delivered by cesarean section (capillary counts) are compared with similar values for normally born infants. The capillary erythrocyte counts are uniformly higher than the erythrocyte counts on the cord blood. Averages show that capillary counts exceed cord counts by 1,000,000 cells per cubic millimeter in normally born infants and by 700,000 in infants born by cesarean section.

The polycythemia of the newborn in our series is not evident. The shock factor due to birth trauma during labor may account for the increased red cell counts.

Values for the copper, iron and hemoglobin contents of cord blood in the two groups are compared. No appreciable difference is noted.

The concentration of iron in the whole blood of the newborn is high, and the amount of copper is low. The iron content is low or normal in the blood of the mothers, and the copper content is high. Copper is needed for the fetal storehouses.

Drs. C. W. Pollard, R. Luikart, E. C. Sage, J. K. Muldoon, L. O. Hoffman, C. Moon, H. E. Anderson, F. Murphy and M. E. Grier supplied us with the samples of blood for analysis.

28. Robertson, O. H., and Bock, A. V., in Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions: Wound Shock and Haemorrhage, Medical Research Committee, Special Report Series, no. 25, London, His Majesty's Stationery Office, 1919, p. 176.

29. Cohnstein, J., and Zuntz, N.: Arch. f. d. ges. Physiol. **42**:326, 1888; cited by Cannon, Fraser and Hooper.[27]

30. Suggs, W. D.: Neo-Natal Shock and Asphyxia, Virginia M. Monthly **61**: 97, 1934.

HUMAN PASSIVE TRANSFER ANTIBODY

IV. STUDIES ON CHILDREN HYPERSENSITIVE TO FOODS

VERNON W. LIPPARD, M.D.
AND
WILLIAM M. SCHMIDT, M.D.
NEW YORK

Weil,[1] Coca [2] and von Fenyvessy and Freund [3] have shown that the anaphylactic state is still demonstrable after anaphylactic antibodies are removed from the blood. Since hypersensitiveness can be transferred by antibodies, they must be associated with the anaphylactic state, but only after they reach the tissues.

The assumption that circulating antibodies protect sensitized tissues from anaphylaxis is paradoxic to the evidence that they induce sensitization. In a recent communication [4] we presented suggestive evidence of protection by human passive transfer antibody. The blood serums of a group of patients with hay fever were titrated by a technic which depends on neutralization of antibody by antigen. It was observed that the antibody titer increased after injection of pollen extracts in 16 of 18 patients and that relief from clinical symptoms of hay fever was associated with a rise in titer. Two patients who showed no rise in titer had severe clinical symptoms despite treatment. In 10 untreated controls the titer remained relatively unchanged during a similar interval. By means of a similar technic, Woringer [5] observed an increase in passive transfer antibody for egg white after subcutaneous injection of specific antigen in 3 eczematous infants.

From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Weil, R.: The Nature of Anaphylaxis and the Relations Between Anaphylaxis and Immunity, J. M. Research **27**:497, 1913.

2. Coca, A. F.: The Site of Reaction in Anaphylactic Shock, Ztschr. f. Immunitätsforsch. u. exper. Therap. **20**:622, 1914.

3. von Fenyvessy, B., and Freund, J.: Ueber den Mechanismus der Anaphylaxie, Ztschr. f. Immunitätsforsch. u. exper. Therap. **22**:59, 1914.

4. Schmidt, W. M., and Lippard, V. W.: Human Passive Transfer Antibody: III. Serial Titrations on Treated and Untreated Patients with Hay Fever, Am. J. Dis. Child. **56**:550 (Sept.) 1938.

5. Woringer, P.: Méthode de dosage de l'anticorps ovalbuminique dans le sang des sujets allergiques au blanc d'oeuf, Ann. Inst. Pasteur **50**:270, 1933.

The purpose of this investigation was to study the response of the passive transfer antibody titer to ingestion of foods in hypersensitive children and to assess the hypothesis that an increase in titer is associated with relief from clinical symptoms after subsequent exposure.

METHOD

A method of titrating the passive transfer antibody by neutralization was described in a previous communication.[6] It was found applicable to the study of antibodies specific for a variety of antigens. The technic is briefly as follows: 1. Constant amounts of serum are mixed with progressive dilutions of antigen. 2. After storage for twenty-four hours, the resultant mixtures are injected intracutaneously into 3 normal recipients. 3. After at least twenty-four hours, antigen is injected intramuscularly. 4. Within twenty minutes to two hours, urticarial reactions appear at the sites prepared with mixtures containing insufficient antigen to neutralize the available antibody completely. 5. The titer of the serum is based on the amount of antigen in the first nonreacting site.

One unit of passive transfer antibody is defined as the amount neutralized by the quantity of antigen that contains 0.00001 mg. of total nitrogen. The titer of a serum is recorded as the number of units of antibody per cubic centimeter of antigen-antibody mixture.

The potency of antigen expressed in terms of nitrogen content may depend on the method of preparation. The results cannot be compared directly with those obtained with different preparations. For this reason one set of antigens was used throughout the study. The peanut antigen was prepared by extraction with buffered saline solution after removal of fat by ether. A dilution of egg white prepared by mixture of several hens' eggs was stored in sealed glass ampules.

RESULTS

The blood serums of a group of children sensitive to foods were titrated repeatedly over long periods. On several occasions, specific antigens were administered under observation in order to determine the effect of ingested antigen on the antibody titer and the influence of elevated titers on the character of clinical reactions following exposure. Food-sensitive patients are less desirable than pollen-sensitive patients for studies of this type because they are not subject to clearly defined periods of natural exposure. This fact probably accounts for the scarcity of previous attempts to analyze fluctuations of passive transfer antibody in this group.

REPORT OF CASES

CASE 1.—W. B., aged 4 years, had infantile eczema at the age of 2 months. Eczema was subsequently limited to the extremities; the condition persisted. At the age of 2 years, the boy had urticaria and angioneurotic edema after eating peanut butter. After the age of 14 months he also had frequent asthmatic attacks associated with infections of the upper respiratory tract and possibly with the inhalation of animal danders, to which his reactions were questionably positive

6. Lippard, V. W., and Schmidt, W. M.: Human Passive Transfer Antibody: I. Titration by Neutralization, Am. J. Dis. Child. **54**:288 (Aug.) 1937.

on intracutaneous tests. Except when ingested under observation, peanut was eliminated from the diet during the period of study.

Fluctuations in titer of passive transfer antibody specific for peanut are shown in chart 1. After the ingestion of twelve peanuts, the patient had urticaria and angioneurotic edema. Within twenty days his antibody titer rose from 60 to 300 units. Ingestion of similar quantities of peanut on three occasions during the next two months, when the titer remained at a level of 150 to 300 units, resulted in neither clinical reactions nor increase in titer. When the child was seen five months later, the titer was 150 units, but it decreased during the next month. When the titer was at a level of 3 units, ingestion of thirty-six peanuts produced a clinical reaction and subsequent increase of titer to 300 units. Ingestion of identical quantities of peanut on two subsequent occasions, when the titer was 150 to 300 units, was followed by neither clinical symptoms nor an increase in titer.

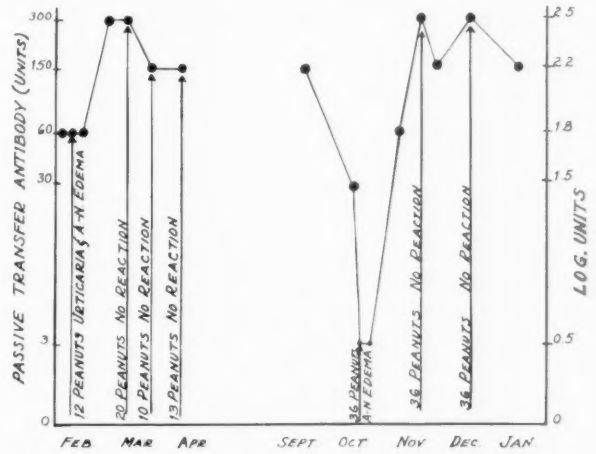

Chart 1 (case 1).—Titer of passive transfer antibody for peanut.

Case 2.—J. S., aged 3 years, had a history of eczema since the age of 2 months and of asthma since the age of 13 months. Intracutaneous tests at the age of 2 years revealed definite hypersensitivity to egg and peanut and questionable reactions to a number of other antigens. Subsequent tests revealed other definitely positive reactions. Peanut and egg were eliminated from her diet during the period of study. It was impossible to keep her in the hospital during the entire interval, however, and she may have ingested small quantities of these foods when at home.

Observations on J. S., who was followed over a period of eighteen months, are shown in chart 2. The ingestion of two peanuts and one week later of eight peanuts produced clinical symptoms on both occasions and a sharp increase in titer from 150 to 1,500 units. After one month the titer decreased, and without stimulation it remained at a lower level for four months. Shortly after ingestion of egg white, a rise in titer of antibody for peanut occurred, the significance of which remains unexplained. Ingestion of twenty-six to twenty-eight peanuts on three subsequent occasions, when the antibody titer ranged between 1,500 and 6,000 units, produced minimal or no clinical response, although the titer increased sharply when the antigen was not vomited. Ingestion of egg white led to the development

of asthma, vomiting and an increase in titer. Otherwise, remarkable fluctuations in titer of antibody for egg white were not observed.

Case 3.—I. W., aged 11 years, had had infantile eczema. Since infancy he had been hypersensitive to egg, and on several occasions urticaria, vomiting and diarrhea followed ingestion of small quantities. His parents reported that he had been on an egg-free diet for a number of years.

In April 1935, at the age of 10 years, the boy contracted acute glomerulonephritis; there was gradual subsidence of symptoms for about a month. In September 1935 the child had a recurrence of the disease; he was admitted to the New York Hospital two months later, with edema and ascites. The clinical

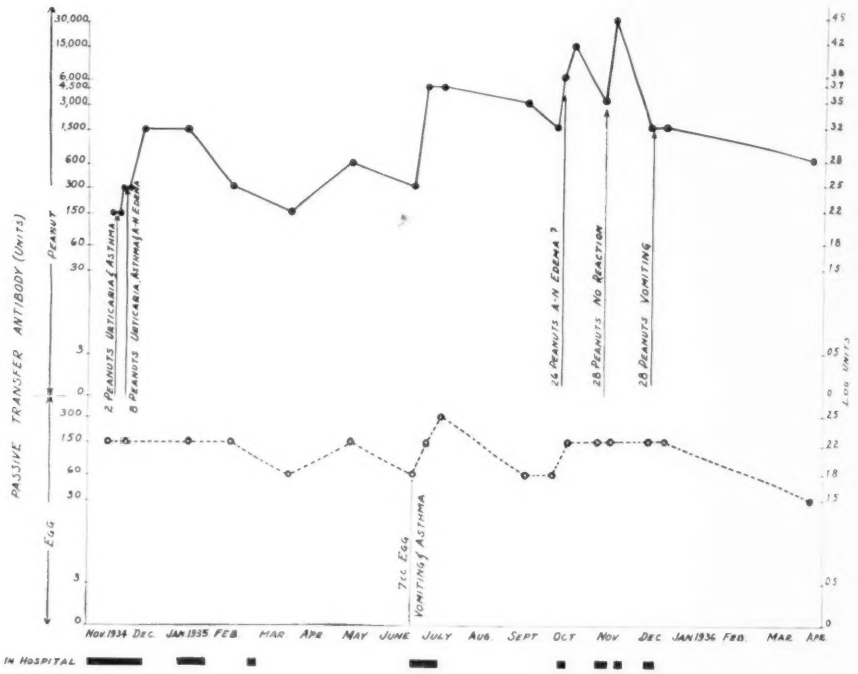

Chart 2 (case 2).—Titer of passive transfer antibody for peanut and for egg white.

picture on his admission was essentially that of subacute glomerulonephritis of nephrotic type. Symptoms subsided in a few weeks, although albuminuria and hypercholesteremia persisted. In January 1936 the boy had a severe infection of the upper respiratory tract and gradually increasing edema. When readmitted to the hospital on February 6 he had generalized edema and ascites. His urine contained a large amount of albumin and erythrocytes, leukocytes and casts.

On February 7 a specimen of blood was obtained, and the patient was given approximately 0.016 mg. of protein from egg white as an intracutaneous test. The antibody titer at that time was at the low level of 30 units. Within fifteen minutes there developed a positive cutaneous reaction, generalized urticaria, coughing and pallor, all of which disappeared promptly on injection of a solution of epinephrine hydrochloride. Within a few hours diuresis began, and during the

next seventeen days the patient's weight decreased from 35.7 to 28.2 Kg. The values of the blood serum proteins were normal by March and those of the blood cholesterol by July. Albuminuria gradually disappeared, and Addis counts of the urinary sediment reached normal levels by October. The boy has remained in good health during the eighteen months since the reaction.

A curve of the antibody titer for egg white in this case is shown in chart 3. There was a prompt increase from 30 to 300 units in seven days after intracutaneous injection of 0.016 mg. of protein from egg white, and the titer ranged between 150 and 300 units during the following three months. Spontaneous remissions are frequently observed in cases of nephrosis, and the improvement in the patient is recorded because of its interest and not because of the conviction that it was necessarily related to the anaphylactic reaction.

Case 4.—E. G., aged 10 months, had received breast milk for two months, and other foods were added at the usual times. She developed normally and had no illnesses. In January 1936, when the infant was 6 months old, her mother fed her a small amount of hard-boiled egg yolk, which she vomited

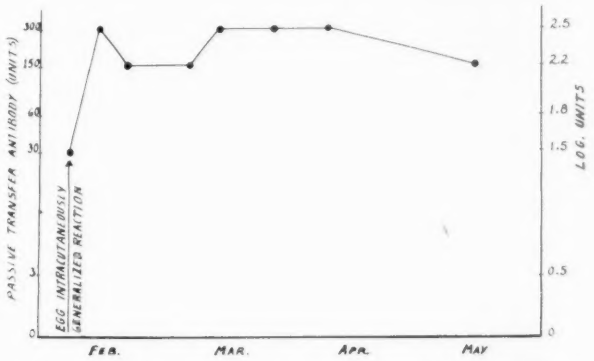

Chart 3 (case 3).—Titer of passive transfer antibody for egg white.

immediately. Two weeks later she received a small amount of soft-boiled egg, which was also vomited. In February a raw egg was added to her formula. A few minutes after eating she vomited and became pale and apathetic. The reaction lasted for about thirty minutes. The infant never had eczema and never vomited or had syncopal attacks except after ingestion of egg. She came under observation on April 8 and was admitted to the New York Hospital.

The results of a series of observations on this patient are recorded in the accompanying table. The history suggests that hypersensitiveness of tissue and clinical hypersensitiveness were present prior to the period of observation. Contact with antigen was followed by the transient appearance of circulating passive transfer antibody. The following controls eliminate the possibility that the "positive" serum (April 21) was demonstrated by injection into an unusually receptive skin: First, all determinations were done on 3 recipients; and, second, "positive" and "negative" serums obtained from this patient were tested simultaneously by local and by intramuscular injection of antigen in the same recipients.

Observations on a group of eczematous infants gave analogous results. In several instances passive transfer antibody specific for egg

white was noted for the first time shortly after the initial ingestion of egg. In these infants, however, it could be demonstrated repeatedly for several months at least. The transient appearance of passive transfer antibody shortly after administration of antigen is also frequently demonstrable in patients who are suffering from serum sickness following therapeutic injection of horse serum.[7]

These observations lead to the conclusion that the passive transfer antibody is not present in the blood stream in constant amounts but is subject to wide variation. The persistence of tissue hypersensitiveness, regardless of the fluctuations and transient appearance of circulating antibody, suggests that in hypersensitive persons antibody may be fixed to the tissues and that if it is coincidentally present in the blood the quantities may be too minute to be detected by available methods.

Immunologic Response to Ingestion of Egg White in Case 4

Date	Amount of Egg White Ingested, Cc.	Clinical Reaction	Passive Transfer Antibody (Units)	Results of Intracutaneous Test	Results of Precipitin Test for Antibodies to Egg White
4/ 8	..	.....	0	..	0
4/10	16	None.....	..	+	..
4/11	15	Pallor, wheezing respiration			
4/13	15	Projectile vomiting			
4/16	..	.....	0	+	0
4/21	..	.....	300	+	0
5/11	5	Vomiting.....	0	+	0
6/12	..	.....	0	..	0
9/15	..	.....	0	+	0

COMMENT

Although comparatively few patients were studied, 63 titrations were done in triplicate and at frequent intervals over periods of several months. Compared with data from animal experiments, in which the large groups of subjects may be sensitized and shocked at will, the observations recorded were definitely limited, but they served to throw some light on the fundamental mechanism of hypersensitiveness in human beings.

These observations suggested, first, that the passive transfer antibody may increase in response to stimulation and, second, that freedom from clinical symptoms following subsequent contact with antigen may be associated with an increase in titer.

7. Longcope, W. T., and Rackemann, F. M.: The Relation of Circulating Antibodies to Serum Disease, J. Exper. Med. **27**:341, 1918. Cooke, R. A., and Spain, W. C.: Studies in Hypersensitiveness: XXXVI. A Comparative Study of Antibodies Occurring in Anaphylaxis, Serum Disease and Naturally Sensitive Man, J. Immunol. **17**:295, 1929.

As early as 1914, Weil [8] concluded that circulating antibody capable of sensitizing may also protect sensitized animal tissues from reaction. He based this conclusion on the observation that sensitized guinea pigs could be partially protected against anaphylactic reactions to intravenous injections of antigen if they were previously given large doses of immune serum. Further, their tissues were not desensitized by an amount of antigen, given subcutaneously, which completely desensitized control animals. Weil's conclusions were supported by Manwaring and Kusama,[9] Dale and Kellaway [10] and Sugg, Richardson and Neill.[11] Recently Morris [12] performed similar experiments and was unable to demonstrate protection of passively sensitized guinea pigs when additional specific immune serum was injected intravenously twenty to sixty minutes before intravenous injection of antigen. Conditions in experimental animals in which comparatively large doses of antigen are introduced by the intravenous route are not analogous to conditions which exist in human beings in whom minute amounts of antigen are absorbed slowly from the respiratory or the gastrointestinal tract when circulating blood contains large amounts of specific antibody. Consequently, it is difficult to apply the results of animal experiments to problems of hypersensitiveness in human beings.

Wells [13] has pointed out that animals may become refractory to anaphylactic reactions in several ways: (1) desensitization through exhaustion of fixed cellular antibodies by their union with antigen; (2) antianaphylaxis when there are sufficient free antibodies in the circulating blood to unite with all the antigen, so that it cannot reach the sensitized tissues; (3) antisensitization against passive anaphylaxis when the blood contains antibodies against the anaphylactic sensitizer (sensitizing serum from an animal of different species), and (4) tissue inactivation when through exhaustion, action of drugs or other injury the sensitized cells cannot respond to the antigen-antibody reaction.

8. Weil, R.: Studies in Anaphylaxis: VIII, J. M. Research **30**:317, 1914.

9. Manwaring, W. H., and Kusama, Y.: Analysis of the Anaphylactic and Immune Reactions by Means of the Isolated Guinea-Pig Lungs, J. Immunol. **2**: 157, 1917.

10. Dale, H. H., and Kellaway, C. H.: Anaphylaxis and Immunity "in Vitro," J. Physiol. **54**:cxliii, 1921.

11. Sugg, J. Y.; Richardson, L. V., and Neill, J. M.: Hypersensitiveness to Diphtheria Bacterial Products: Inhibition of the Anaphylaxis of Antitoxic Immune (Actively Sensitized) Guinea Pigs, J. Immunol. **20**:25, 1931.

12. Morris, M. C.: The Relation Between Antianaphylaxis and Antibody Balance: I. The Role of Excess Circulating Antibody in Hypersensitiveness, J. Exper. Med. **64**:641, 1936; II. The Effect of Specific Desensitization upon Resistance to Infection and upon Antibody Balance, ibid. **64**:657, 1936.

13. Wells, H. G.: Chemical Aspects of Immunity, New York, The Chemical Catalogue Company, 1929, p. 221.

If one applies these concepts to hypersensitiveness in human beings, it becomes obvious that antisensitization plays no role and that, under the conditions of these experiments, neither is tissue inactivation a factor. Tissue hypersensitiveness, demonstrated by intracutaneous reactions, persisted throughout the periods of observation in both the food-sensitive and the pollen-sensitive patients. Therefore, these patients were not desensitized.

The remaining mechanism is that which Wells designated as anti-anaphylaxis. If this principle is applied to hypersensitiveness in human beings, it must be assumed that the hypersensitive tissues are protected from anaphylaxis when circulating antibody is present in amounts sufficient to neutralize the absorbed antigen. Although absence of detectable passive transfer antibody may be assumed to represent the normal state, in the presence of hypersensitiveness protection may be closely associated with an increased titer. It was shown that an increase in antibody titer was associated with relative freedom from clinical symptoms when specific antigen was subsequently ingested or inhaled. Furthermore, quantitative studies [14] have previously demonstrated that antigen may be neutralized by specific human passive transfer antibody. It is conceivable, therefore, that at least one of the mechanisms of protection in human hypersensitiveness may depend on neutralization of antigen by circulating antibody. This increase in antibody titer is only one factor; other as yet unrecognized factors may be of equal importance.

SUMMARY AND CONCLUSIONS

Blood serums of children hypersensitive to foods were titrated for passive transfer antibody by a method which depends on neutralization of antibody by its specific antigen.

Ingestion of foods to which patients were hypersensitive was followed by increase in titer of passive transfer antibody when antigen sufficient to produce clinical reactions was absorbed. The absorption of specific antigen is therefore capable of augmenting the production or mobilization of this antibody in the blood serum.

Clinical reactions to absorption of specific foods were less frequently observed and less pronounced after an increase in titer of passive transfer antibody. This evidence suggests that in human beings protection of sensitized tissues from manifestations of hypersensitiveness may be associated with a rise in titer of circulating passive transfer antibody.

525 East Sixty-Eighth Street.

14. Schmidt, W. M., and Lippard, V. W.: Human Passive Transfer Antibody: II. Neutralization of Antigen, Am. J. Dis. Child. **54**:777 (Oct.) 1937.

EFFECT OF A MILK SUPPLEMENT ON THE PHYSICAL STATUS OF INSTITUTIONAL CHILDREN

III. PROGRESS OF DENTAL CARIES

LYDIA J. ROBERTS, PH.D.

STELLA ENGLEBRECHT, S.M.

RUTH BLAIR, S.M.

WARREN WILLIAMS, D.D.S.

AND

MARGUERITE SCOTT, S.M.

CHICAGO

The two preceding articles in this series [1] have shown that the daily addition of a pint (473 cc.) equivalent of evaporated milk to the diets of children in an institution (one group receiving irradiated and the other nonirradiated milk) produced a measurable increase of growth in height and weight and in ossification of the bones in the wrists as compared with that of the control group given the regular institutional diet. The present study deals with the progress of dental caries in the same groups of children during the same period.

LITERATURE

A number of workers have reported a striking arrest of dental caries as a result of different types of dietary supplement. Since their findings have been reviewed many times (Hanke,[2] 1934) they will be only briefly

The expenses of this investigation were defrayed in part by the Irradiated Evaporated Milk Institute.

From the Nutrition Laboratory, Department of Home Economics, University of Chicago, and the Chicago College of Dental Surgery, Dental Department of Loyola University.

1. Roberts, L. J.; Blair, R.; Lenning, B., and Scott, M.: Effect of a Milk Supplement on the Physical Status of Institutional Children: I. Growth in Height and Weight, Am. J. Dis. Child. **56**:287 (Aug.) 1938. MacNair, V., and Roberts, L. J.: Effect of a Milk Supplement on the Physical Status of Institutional Children: II. Ossification of the Bones of the Wrist, ibid. **56**:494 (Sept.) 1938.

2. Hanke, M. T.: Rôle of Diet in the Cause, Prevention, and Cure of Dental Diseases, J. Nutrition **3**:433 (Jan.) 1931.

recalled here. Mellanby, Pattison and Proud,[3] working with children in an institution, were the first to show experimentally that the incidence of caries could be reduced by a diet containing liberal amounts of milk, eggs and cod liver oil and small amounts of cereal. Later Mellanby and Pattison [4] extended these experiments and attempted to determine the factors involved. They found that a liberal fortification of the basic diet with vitamin D caused a marked reduction in the spread of caries and that when this therapy was combined with a cereal-free diet rich in calcium the initiation and spread of caries were almost eliminated. They stated the belief that all three factors—vitamin D, calcium and restriction of cereals—are important in controlling decay.

Boyd, Drain and Nelson [5] reported arrest of caries in children given diets differing widely in type: (1) the diet for diabetic children (low carbohydrate and high fat content and liberal quantities of succulent vegetables), (2) the diet for children with celiac disease (high in protein and low in starches and fats and in the usual fruits and vegetables) and (3) the ordinary mixed diet for children at its best (one containing all the foods prescribed by nutritionists to cover liberally the child's nutritional requirements). In spite of the apparent differences in these diets it will be noted that they have one thing in common; namely, they all provide generous amounts of all the known dietary essentials. These workers therefore stressed the importance of a diet adequate in all respects in arresting decay.

It is of interest to note that retardation of dental caries can also be effected through the type of general dietary supervision which can be given to outpatients in a dental clinic. Howe, White and Rabine [6] reported a reduction of 79 per cent in dental caries in 104 cooperative patients over a period of one and six-tenths years, while 28 uncooperative patients had an increase of 13 per cent, the normal expectancy for the period.

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3. Mellanby, M.; Pattison, C. L., and Proud, J. W.: Effect of Diet on the Development and Extension of Caries in the Teeth of Children, Brit. M. J. **2**: 354 (Aug. 30) 1924.

4. Mellanby, M., and Pattison, C. L.: Some Factors Influencing the Spread of Caries in Children, Brit. Dent. J. **47**:1045, 1926; Action of Vitamin D in Preventing the Spread and Promoting the Arrest of Caries in Children, Brit. M. J. **2**:1079 (Dec. 15) 1928; Influence of a Cereal-Free Diet Rich in Vitamin D and Calcium on Dental Caries in Children, ibid. **1**:507 (March 19) 1932.

5. Boyd, J. D., and Drain, C. L.: Arrest of Dental Caries in Childhood, J. A. M. A. **90**:1867 (June 9) 1928. Boyd, J. D.; Drain, C. L., and Nelson, M. V.: Dietary Control of Dental Caries, Am. J. Dis. Child. **38**:721 (Oct.) 1929. Drain, C. L., and Boyd, J. D.: Control and Arrest of Dental Caries: Institutional Study, J. Am. Dent. A. **22**:155 (Jan.) 1935.

6. Howe, P. R.; White, R. L., and Rabine, M.: Retardation of Dental Caries in Outpatients of a Dental Infirmary, Am. J. Dis. Child. **46**:1045 (Nov., pt. 1) 1933.

Bunting, Koehne, Jay and their co-workers,[7] at the University of Michigan, observed the effect of various dietary regimens on the incidence of caries in large numbers of children. These studies were made in several institutions, in public schools and also under controlled experimental conditions in the laboratory. To summarize, the results of all these investigations have unfailingly shown that children given a good or even a moderately well balanced diet that is low in sugar have remained remarkably free from caries for several years. Moreover, even rampant caries has been brought under control in other groups by introducing this same dietary program. The one outstanding difference, in brief, between the diets that favor and those that inhibit dental caries is the amount of sugar in the form of sweetened foods and candy. These authors expressed the belief that sugar favors the development of Bacillus acidophilus and that it is the activity of this organism that is largely responsible for the initiation and spread of dental caries.

The Dental Research Group at Columbia University, as reported by McBeath [8] and Hollander,[9] tested the influence of several nutritional procedures on the spread of dental caries in children in a number of orphanages. These procedures included: (1) additions to the basal diet of the institution to make it the equivalent of the optimal diet for children as used by Boyd, Drain and Nelson; (2) vitamin D therapy, the vitamin being supplied either in viosterol, in vitamin D milk or by irradiation, and (3) addition of vitamin C. It was observed that the incidence of caries was markedly reduced both by the all-around adequate diet and by the basal diet supplemented solely by some form of vitamin D. In from 40 to 60 per cent of children so treated caries was completely arrested. Ultraviolet irradiation proved more effective than other methods of supplying vitamin D. Additions of liberal amounts of vitamin C in several forms had little effect on the incidence of caries,

7. Bunting, R. W.; Jay, P., and Hard, D. G.: Report of the Successful Control of Dental Caries in Three Public Institutions, J. Am. Dent. A. **18**:672 (April) 1931. Koehne, M.; Bunting, R. W., and Morrell, E.: Control of Dental Caries in Children, Am. J. Dis. Child. **48**:6 (July) 1934. Koehne, M., and Bunting, R. W.: Studies in the Control of Dental Caries, J. Nutrition **7**:657 (June) 1934. Bunting, R. W.: Bacteriological, Chemical, and Nutritional Studies of Dental Caries by the Michigan Research Group, J. Dent. Research **14**:97 (April) 1934. Jay, P.; Hadley, F. P., and Bunting, R. W.: Observations on the Relation of Lactobacillus Acidophilus to Dental Caries in Children During Experimental Feeding of Candy, J. Am. Dent. A. **23**:846 (May) 1936.

8. McBeath, E. C.: Nutritional Control of Dental Caries, New York State J. Med. **33**:1086 (Sept. 15) 1933; Experiments on Dietary Control of Dental Caries in Children, J. Dent. Research **12**:723 (Oct.) 1932; Vitamin D Studies, Am. J. Pub. Health **24**:1028 (Oct.) 1934.

9. Hollander, F.: Coordinated Report of the Columbia University Dental Caries Research Group, J. Dent. Research **14**:303 (Aug.) 1934.

and the authors stated the opinion, therefore, that lack of this vitamin cannot be responsible for the great susceptibility to dental decay.

Contrary findings for the efficacy of vitamin C in arresting decay are reported by Hanke [10] as the result of a two-year study at Mooseheart, Ill. During a one year control period, 79.2 per cent of the children showed progressive caries and 70.9 per cent some type of inflammation of the gums. The daily addition to their diet of 1 pint of orange juice and the juice of one lemon during the second year "led to an almost complete disappearance of gum inflammation, a 50 per cent reduction in the incidence of dental caries and an acceleration in the rate of growth."

In the outpatient department of a dental clinic, Schoenthal and Brodsky [11] tested the effect of irradiation and administration of viosterol on the development of caries in 319 children from 6 to 14 years of age. Each type of therapy was employed both for children given good diets and for those given poor ones. The results showed that vitamin D plays a definite role in control of caries only when the diet is generally poor. In 60 per cent of the children supplied with good diets, either with or without viosterol or irradiation, no new cavities developed. In the groups with poor diets, 68 per cent of those having vitamin D therapy had no advance in caries, as compared with 40 per cent of the control group. Addition of fruit alone to a poor diet was ineffective. The authors stated that the children were also given prophylactic treatment throughout the study and that oral hygiene therefore shows a possible relation to the control of dental caries.

The influence of the fat-soluble vitamins on the carious process when they are administered as the only dietary supplement has been investigated by Day and Sedwick [12] in 500 seventh grade pupils in a public school. After a careful initial clinical examination, supplemented by roentgenographic exposures of every tooth, the children were divided into two comparable groups. One remained as a control. In the other group, each child received daily a vitamin tablet which supplied not less than 6,000 U. S. P. units of vitamin A and 3,780 U. S. P. (1,400 Steenbock) units of vitamin D. At the end of the school year a reexamination was made by the same method, and the two groups were compared for number of new teeth affected, number of new cavities and increase in the "caries figure." The results were almost identical for

10. Hanke, M. T., and others: Nutritional Studies on Children, Internat. J. Orthodontia **19**:642 (June) 1933.

11. Schoenthal, L., and Brodsky, R. H.: Dietary Control and Etiology of Dental Caries, Am. J. Dis. Child. **46**:91 (July) 1933.

12. Day, C. D. M., and Sedwick, H. J.: (*a*) Fat Soluble Vitamins and Dental Caries in Children, J. Nutrition **8**:309 (Sept.) 1934; (*b*) Studies on the Incidence of Dental Caries, Dental Cosmos **77**:442, 1935.

the two groups and indicate therefore (contrary to the findings of Schoenthal and Brodsky [11]) that vitamin D alone added to a poor diet is ineffective in arresting decay. The authors expressed the belief that faith should be put in a completely adequate diet rather than in any one supplement.

More promising results from vitamin D therapy have been reported by Anderson and others [13] from a study of 162 children in two orphanages in Toronto. One group was given 8 drops daily of viosterol containing 10,000 U. S. P. units of vitamin D per gram; the other was the control group. The diets were otherwise good, and oral and general hygienic habits were satisfactory. At the end of a year the results showed a definite inhibiting effect of vitamin D on the progress of caries. The average number of new cavities which had developed was less than half as many in the experimental as in the control group. Jameson and Cox [14] also reported beneficial results from daily administration of a vitamin D concentrate to a small group of children in a New Zealand orphanage as compared with the results in a control group, which showed definitely progressive caries.

It is clear from the foregoing review that a considerable group of workers have found that diet does in some way play a role in the retardation of dental caries, but the factors chiefly involved in inhibiting decay and their mode of action are not as yet matters of general agreement. Some authors have put their faith in vitamin D, others in vitamin C and still others in restriction of sweets. A larger number, perhaps, have stated the belief that only a well balanced diet which is liberally fortified with all needed minerals and vitamins and which has a low content of sugar can be depended on to favor the development and preservation of the dental structures.

The present investigation afforded the opportunity to test the effect of adding the dietary constituents contained in a pint of milk per child per day to a diet already containing a scant pint and also to determine whether the amount of vitamin D contained in irradiated milk (about 70 units per pint) would have any inhibiting effect on dental decay.

SUBJECTS

The subjects of this study were approximately the same as those used in the two preceding studies. They differed in a few cases because an occasional child might have been present for one of the final measures but not for the others. Initial examinations were made of the teeth of 144 children. Of this group, only 106 were still in the institution and available for examination at the close of the year's

13. Anderson, P. G., and others: The Influence of Vitamin D in the Prevention of Dental Caries, J. Am. Dent. A. **21**:1349 (Aug.) 1934.

14. Jameson, A. B., and Cox, H.: Clinical Note on Vitamin D and Dental Caries, New Zealand M. J. **32**:41 (Feb.) 1933.

experiment. Of the original trios chosen on the basis of age, sex and condition of teeth, 30 remained complete at the end. The data for the original group of 144 show the condition of the teeth in the institution at the beginning. For judging the effect of the supplement on the progress of dental caries only the data for the 90 children in the 30 matched trios are utilized.

DENTAL INSPECTION AND RECORDING

Every child was submitted to a detailed dental inspection at the beginning and again at the close of the year of study. The examinations were made by a dentist with wide experience in examining children's teeth. Charts were prepared with outlines of the teeth drawn four times their natural size. The cavities were outlined with ink, their exact location and relative size being shown. Drawings of mesial and distal views were inserted when cavities were found on these surfaces alone. A seven point rating scale was devised for expressing the degree of decay numerically, and the criteria for the classification were objectively described as follows:

0. Virtual certainty of no decay
1. Pits, fissures or stained shadowed areas suspected of being carious
2. Shallow cavities, extending just to the dentin
3. Medium cavities, extending midway through the dentin
4. Deep cavities, not quite involving the pulp
5. Cavities exposing vital pulp
6. Cavities exposing gangrenous pulp

6R. Only roots left

Roentgenograms were made of all teeth on the initial examination and were checked against the dentist's findings. Cavities revealed by this method and not found by the dentist were entered on the chart in different-colored ink in order to make possible a comparison of the findings by the two methods.

During the experimental year the children continued with approximately the same type of dental service they had formerly had. The institution employed no regular dentist but utilized volunteer service of several dentists in the neighborhood for the most urgent demands. The institution was, indeed, selected because of the relatively small amount of dental care given there. To test the effect of the dietary supplement on arrest or spread of caries, it was desirable to leave the teeth otherwise largely untreated. While one could not in conscience, then, deliberately omit dental service for children already well cared for, it seemed justifiable to choose a group of children whose teeth were already being neglected and to allow the situation to continue for one more year. The dentists continued to give care in emergencies, filling the worst cavities and extracting teeth which were past saving or which were causing trouble. Even with this program there still remained a sufficient number of untreated teeth on which to determine the spread of caries under the three dietary regimens.

At the end of the year a reexamination was made of the teeth of the 106 children of the original group who still remained; this was done by the same dentist and by the same method employed at the beginning, save that roentgenograms were omitted. This omsision was decided on as an economy measure which seemed justified on the basis of the findings on the first examination. Day and Sedwick [12a] had reported that from 26 to 29 per cent of 2,264 cavities would have

been missed in their study if the roentgen study had been omitted, while Delabarre [15] found that 50 per cent of 3,802 cavities would have been overlooked without the roentgen findings. In the present study there was no such discrepancy between the results obtained by the two methods. Clinical examination revealed 1,599 cavities; roentgen study added only 80 to this number. The percentage which would have been missed without roentgen study therefore was 3.7. Moreover, 30 of the 80 cavities were of size 1 or doubtful. Omitting these leaves but 3 per cent of real cavities which would have been overlooked. In addition to the 80 cavities missed there were 15 cavities regarding which the judgment as to size was changed on the basis of the roentgen study. If these are added to the 80 missed on clinical examination there was a total of 95 errors in judgment, or 5.6 per cent. In a more recent report, moreover, Day and Sedwick [12b] reported only 5 per cent of cavities missed, a close agreement with the results for the present study. In view of these results and of the finding of Day and Sedwick that the error from missed cavities would have been almost the same for control and for experimental groups, it seemed justifiable to omit the roentgen study on the final examination.

TABLE 1.—*Condition of Teeth of One Hundred and Forty-Four Children at Beginning of Study*

Teeth	Total*		Deciduous		Permanent	
	No.	%	No.	%	No.	%
All	3,457	100.0	1,039	100	2,418	100
Present and sound	2,252	65.1	560	54	1,692	70
Decayed, including permanent extracted	1,205	34.9	479	46	726	30
Lost	49	1.4	.....	...	49	2
Decayed	1,156	33.5	479	46	677	28
Filled, no further decay	74	2.1	11	1	63	3
Filled, further decay	116	3.6	32	3	84	4
Unfilled	966	27.9	436	42	530	22

* Total includes all teeth present plus lost permanent teeth. It disregards 119 lost temporary teeth not replaced by permanent teeth.

A distinguishing feature of this study was that entirely new record sheets were used for the final examinations, the dentist not having access to the initial records until after the examinations were completed. He had not, as a matter of fact, even seen the original records for more than nine months prior to the final checking. The complete independence of these two examinations was deemed essential to the accuracy of the results. The method is, of course, a severe test of the objectivity and consistency of the examiner's ratings, but for this very reason it should be employed in studies of this type, in which a subjective element is of necessity involved. In the present instance the remarkable consistency between the initial and the final records of the examinations furnished the best evidence that could have been obtained of the accuracy and the objectivity of the examiner's ratings.

CONDITION OF TEETH AT THE BEGINNING OF THE EXPERIMENT

The belief that this was a group of children neglected in respect to dental care was borne out by the results of the initial examinations, as recorded in tables 1 to 3. Counting all teeth present and the perma-

15. Delabarre, F. A.: Preschool Age Dentistry, J. Am. Dent. A. **20**:124 (Jan.) 1933.

nent ones which had been extracted, these 144 children had a total of 3,457 teeth, of which 1,039 were deciduous and 2,418 permanent. More than one third (34.9 per cent) of these were found to be decayed. Most of them, moreover, were either unfilled (27.9 per cent) or had been filled and were further decayed (3.6 per cent). A small fraction only (3.4 per cent) had been filled and had remained sound. A large proportion (60 per cent) of the affected teeth were permanent. Of the 2,418 permanent teeth which had erupted, almost one third (30 per cent) were already decayed. Of these, 49 had been extracted, 530 were unfilled and 84 had been filled but were again decayed. Excluding the filled teeth which remained sound and the missing permanent teeth, there remained a total of 1,082 teeth (614 of which were permanent) which were in need of attention at the time the study was started. The most striking evidence of extreme decay is found in the condition of the first permanent molars. In this group of 144 children 517 of the first permanent molars had erupted. Of these, only 29.4 per cent were still present and sound; the remaining 70.6 per cent, or nearly three fourths, were decayed (63.2 per cent) or had been extracted (7.4 per cent).

The degree of decay is further indicated by the size of the cavities. This has been considered both as to number of teeth affected (table 2) and as to total number of cavities (table 3). Of the 1,082 decayed teeth, one fourth had only cavities of size 1, or doubtful caries. Three fourths of the teeth, however, had real cavities, that is, of size 2 or above. One half of the teeth had cavities of size 3 or larger, and one fourth of size 4 or above. If the teeth with only cavities of size 1 are excluded, there still remain 817 teeth, or 24 per cent of all the teeth, which had real cavities. Considering next the total number of cavities (table 3), 1,679 for all teeth, one third were size 1, two thirds were size 2 or larger and 39 per cent were size 3 or above. Again excluding cavities of size 1, there still remain 1,117 real cavities, an average of 7.7 cavities per child in need of attention. That the cavities of size 1 should probably not be disregarded, however, is indicated by the findings of the present study (reported more fully later) in regard to the state of these cavities a year later. Of 382 cavities of size 1 found for the 90 matched children at the beginning and remaining at the end, 282 (or 74 per cent) had become real cavities (of size 2 or larger) by the end of the year (table 6). This confirms in large measure the dentist's judgment that these cavities of size 1 were potentially cavities of larger size.

The dental status of the children in the institution at the time the study was undertaken can be summed up graphically by observing that had it been planned to put the teeth of all children in the institution in good condition, it would have been necessary to fill 1,679 cavities in

1,082 teeth in the mouths of 144 children. Or, disregarding deciduous teeth, there would still have been 1,019 cavities in 614 permanent teeth to claim attention.

MATCHED GROUPS

As already indicated, there remained at the end of the year 30 trios, consisting of 1 child each from a group of control children, a group who

TABLE 2.—*Size of Cavities in 1,082 Decayed Teeth, the Largest Cavity in Each Tooth Being Measured*

	Total		Deciduous			Permanent		
	No.	%	No.	Percentage of Total	Percentage of Deciduous	No.	Percentage of Total	Percentage of Permanent
Number of teeth*	1,082	100.0	468	43.3	100.0	614	56.7	100.0
Size of cavity in tooth								
1	265	24.6	43	4.0	9.2	223	20.6	36.3
2	270	24.8	103	9.4	22.0	167	15.4	27.2
3	255	23.7	124	11.5	26.5	131	12.1	21.2
4	122	11.3	68	6.4	14.5	54	5.0	8.8
5	72	6.7	51	4.7	10.9	21	1.9	3.5
6	50	4.6	38	3.5	8.1	12	1.1	2.0
6R	13	1.2	12	1.1	2.6	1	0.1	0.2
Arrested (Size undetermined; 3 or larger)	34	3.1	29	2.7	6.2	5	0.5	0.8

* Includes 1,156 decayed teeth minus 74 filled teeth which had no further decay.

TABLE 3.—*All Cavities Classified by Size*

	Total		Deciduous			Permanent		
	No.	%	No.	Percentage of Total	Percentage of Deciduous	No.	Percentage of Total	Percentage of Permanent
All cavities	1,679	100.0	660	39.0	100.0	1,019	61.0	100.0
Size of cavity								
1	562	33.6	93	5.6	14.3	469	28.0	46.0
2	460	27.4	179	10.3	26.5	281	16.9	27.6
3	324	19.3	160	9.5	24.2	164	9.8	16.0
4	135	8.0	74	4.4	11.3	61	3.6	6.0
5	70	4.0	48	2.9	7.5	22	1.3	2.2
6	49	2.9	36	2.2	5.6	13	0.8	1.3
6R	12	0.8	11	0.6	1.6	1	0.1	0.1
Arrested (size undetermined; 3 or larger)	67	4.0	59	3.5	9.0	8	0.5	0.8

received plain milk and a group who received irradiated milk, who were matched as closely as possible at the beginning on the bases of age, sex, degree of carious teeth and other pertinent factors. Accurate matching was, of course, impossible, but the children in each trio were at least of the same sex and in the same period of growth and had the same general type of dental condition; that is, they (1) were relatively immune or had (2) a moderate or (3) an extreme degree of caries. On the basis of this matching there resulted three dietary groups of 30 children each which were closely alike as to dental status when the

study began. This is evidenced by table 4, in which is summarized the average condition of the teeth of the children in each of the three dietary groups at the beginning of the study.

Considering the difficulties involved in such matching, the groups are found to be surprisingly alike in respect to important factors. The average age was 9.6 years for the control, 9.9 for the milk and 10 for the D milk group. The 774 decayed teeth of the 90 children were distributed as follows: 261 for the control, 248 for the milk and 265 for the D milk group, an average of 8.7, 8.3 and 8.8 carious teeth, respectively, per child for the three groups. The 1,080 cavities were similarly almost equally divided among the groups: 352 for the control, 361 for the milk and 367 for the D milk group, or averages of 11.7, 12 and 12.2 cavities per child for the respective groups. The caries scores of the three groups were also in close agreement. This score is arrived at by totaling the size of all cavities. That is, if a child had 3 cavities of

TABLE 4.—*Comparison of Dental Status of Three Matched Groups at Beginning of Experiment*

		Carious Teeth		Cavities		Caries Score	
Average Age in Years		No.	Average Child	No.	Average Child	Total	Average Child
All groups		774	8.6	1,080	12.0	2,497	....
Control	9.6	261	8.7	352	11.7	817	27.2
Milk	9.9	248	8.3	361	12.0	878	29.3
D milk	10.0	265	8.8	367	12.2	802	26.7

size 2, 2 of size 4 and 1 of size 5, his caries score was 19. This is an arbitrary method of expressing degree of decay, but since it was applied impartially to all groups it was probably as fair a means of comparison as could be employed. According to this method the total caries score was 817 for the control, 878 for the milk and 802 for the D milk group; the average scores were 27.2, 29.3 and 26.7 for the respective groups. Considering all the variables involved in such matching, it seems scarcely possible to find three better matched groups than these on which to test the effect of a dietary supplement. As indicated in the earlier articles, one group served as a control, and the other two received an additional pint equivalent of evaporated milk per child, one group having it in the irradiated and the other in the nonirradiated form.

EXTENSION OF CARIOUS CONDITION DURING THE EXPERIMENTAL YEAR

It has been seen that the children in this institution had a marked amount of dental decay at the beginning of the study and that the three groups were closely alike in this respect. To what extent did the con-

dition change during the year, and was there any difference between the three dietary groups? These questions were attacked from several standpoints: (1) the increase in number of decayed teeth, (2) the increase in the number and size of cavities and (3) the advance in the caries score. These points were considered, furthermore, in respect to averages for the entire group of 90 children as well as for each dietary group and for individuals within the groups. The results of these analyses are recorded in tables 4 to 8 and in charts 1 and 2.

The picture presented by these records is outstandingly one of progressive caries for all the groups. Taking first the entire group of 90 children, it is seen (table 5) that at the end of the year they had

TABLE 5.—*Increase in Carious Condition During Year*

		Increase in Number of Carious Teeth			Increase in Number of Cavities			Increase in Caries Score		
	No.	No.	%	Average per Child	No.	%	Average per Child	No.	%	Average per Child
All children	90									
All teeth		197	25.5	2.2	544	50.4	6.0	1,739	97.7	19.3
Deciduous		46			142			555		
Permanent		151			402			1,184		
Control children	30									
All teeth		75	28.7	2.5	112	54.5	6.5	583	109.0	19.4
Deciduous		22			57			192		
Permanent		53			135			391		
Children given milk	30									
All teeth		65	26.2	2.1	166	46.0	5.6	563	92.6	18.7
Deciduous		14			40			175		
Permanent		51			126			388		
Children given D milk	30									
All teeth		57	21.5	1.9	186	50.7	6.2	593	94.6	19.8
Deciduous		10			45			188		
Permanent		47			141			405		

197 more carious teeth than they had at the beginning; 151 of these were permanent teeth. This is an increase of 26 per cent, or an average of 2.2 additional carious teeth per child. The number of cavities increased to an even greater extent; 544 new cavities developed during the year, 402 of them in permanent teeth. This was an increase of 50 per cent, or an average of 6 new cavities per child.

Not only did new cavities develop, however, but old ones increased in size. This can be observed in table 6, in which is shown the number of cavities of each size which remained the same or progressed to the larger sizes. Perhaps one of the most surprising facts revealed by this table is the large proportion of defects of size 1 which became real cavities. As pointed out earlier, three fourths of these (74 per cent) became size 2 or larger; 41 per cent were size 3 or larger, and a con-

siderable number became size 4, 5 or 6 or were even lost by extraction. A similar increase in size was found for other cavities. Two thirds of the cavities formerly size 2 became 3, 4, 5 or 6, and from half to three fourths of those formerly size 3, 4, 5 and 6 progressed to larger sizes or were lost by extraction.

The simplest method of expressing the total change, however, is in terms of the caries score, since this score reflects increase both in number of cavities and in size of old ones (table 5). In the present case the 90 children had an increase of 1,739 points in caries score, an advance of 97.7 per cent or an average of 19.3 points per child. Whatever method of analysis is used, in short, reveals a marked advance in caries score.

This increase in dental destruction was not, moreover, confined to a few children but was common to all the group, though some children

TABLE 6.—*Change in Size of 1,080 Cavities in Teeth of Ninety Children During Experimental Year*

		Percentage Showing Specified Change							
			Increased to Specified Size						
	Total Cavities	No Change	Total	2	3	4	5	6	Extracted	Filled
All cavities	1,080									
Size of cavity at beginning of year										
1	382	26	74	33	22	6	1	*	2	9
2	294	31	69	..	35	11	4	2	6	11
3	221	43	57	..	..	18	7	2	13	17
4	90	33	67	..	..	..	14	6	16	31
5	54	26	74	..	..	..	..	9	41	24
6	39	49	51	..	..	..	..	..	51	..

* Less than 1 per cent.

showed greater advance than others. Although 4 children had immune mouths at the beginning, no child was free from decay at the end. As seen in table 7, in 72 of the 90 children carious points had developed in 1 or more additional teeth, and 13 of these children had 5 or more teeth affected that were sound at the beginning. The spread of caries is even more evident in the number of new cavities which developed during the period. In this respect no child escaped (table 7). Of the 90 children, 34 had acquired less than 5 new cavities; but the remaining 56, almost two thirds of the group, had at least 5 new cavities each, and 18 of these had as many as 10 or more. The total picture is best presented, however, in the caries score (table 7). No child failed to show advance, though 22 (24 per cent) had an increase of less than 10 points. Three fourths of the group advanced 10 or more points: 17 of these by from 20 to 29 points, 9 by from 30 to 39 points and 9 by 40 or more

points. The significance of this increase in score is best comprehended by remembering that 40 points is the equivalent of 10 cavities of size 4 or 20 of size 2.

When the condition of the teeth at the beginning is recalled, it is readily realized that with the year's quota of decay added the teeth of these children were indeed in a sorry plight.

So much for the group as a whole. Our chief interest now centers on the comparison of the three dietary groups. These groups were well matched at the outset and may be considered as having had an even start. The two groups that received the pint of milk supplement were ingesting daily considerable amounts of a number of dietary essentials important for the development of bone and tooth above their former

TABLE 7.—*Percentage of Children in Each Dietary Group Who Had Specified Increase in Carious Condition of Teeth During Experimental Year*

	All Children		Control		Milk		D Milk	
	No.	%	No.	%	No.	%	No.	%
Total children	90	100	30	100	30	100	30	100
Increase in number of carious teeth								
No increase	18	20.0	6	20.0	5	16.7	7	23.3
1-4 teeth	59	65.6	19	63.3	21	70.0	19	63.3
5 or more	13	14.4	5	16.7	4	13.3	4	13.3
Increase in cavities								
None	0	0	0	0	0	0	0	0
1-4 cavities	34	37.8	10	33.3	10	33.3	8	26.6
5-9 cavities	38	42.2	7	23.3	14	46.7	13	43.3
10 and over	18	20.0	13	43.3	6	20.0	9	30.0
Increase in score								
No increase	0	0	0	0	0	0	0	0
Less than 10	22	24.4	8	26.6	9	30.0	5	16.6
10-19	33	36.7	8	26.6	10	33.3	15	50.0
20-29	17	18.9	7	23.3	5	16.7	5	16.6
30-39	9	10.0	6	20.0	3	10.0	0	0
40 and over	9	10.0	1	3.3	3	10.0	5	16.7

supply and above that of the control group. Expressed in quantitative terms, these amounted daily to approximately the following values:

Calories	Protein Gm.	Calcium Gm.	Phosphorus Gm.	Iron Gm.	Vitamin A Units	Vitamin B_1 Units	Vitamin B_2 Units
336	19	0.64	0.49	0.0014	615	47	265

The children receiving irradiated milk were obtaining in addition about 70 units of vitamin D. With this excellent fortification of the diet, it might be expected that the progress of caries would be checked in the groups given a supplement, or at least would be significantly less than for the control group.

A study of tables 5, 7 and 8 and of charts 1 and 2, in which comparison of the three groups has been graphically depicted, shows that there was certainly no appreciable arrest of dental decay in the groups

receiving the supplement. All groups had an extreme degree of decay at the beginning, and the teeth of all were in a much worse condition at the end of the year. The changes for the three groups were moreover in the same direction, and at first glance there appears to be little difference between them. On closer inspection of charts 1 and 2, however, it is noted that by most methods of comparison there does appear to be a slight difference in favor of the children given a supplement. The average increase in number of carious teeth was 2.5 for the control,

TABLE 8.—*Percentage of Times in Thirty Matched Trios That Control Child, Child Given Milk and Child Given D Milk Had Best, Second Best and Poorest Record in Advance in Carious Condition**

	Control		Milk		D Milk	
	No.	%	No.	%	No.	%
Newly carious teeth						
Best	5.5	18.3	7.5	25.0	15.0	50.0
Second best	11.5	38.3	10.0	33.3	6.5	21.6
Poorest	11.0	36.6	10.5	35.0	6.5	21.6
Groups even	2.0	6.6	2.0	6.6	2.0	6.6
Percentage of increase in carious teeth						
Best	9.0	30.0	9.0	30.0	11.0	36.6
Second best	8.0	26.6	12.0	40.0	9.0	30.0
Poorest	12.0	40.0	8.0	26.6	9.0	30.0
Groups even	1.0	3.3	1.0	3.3	1.0	3.3
New caries						
Best	9.5	31.6	10.0	33.3	10.5	35.0
Second best	7.5	25.0	12.5	41.6	10.0	33.3
Poorest	13.0	43.3	7.5	25.0	9.5	31.6
Percentage of increase in caries						
Best	5.5	18.3	12.0	40.0	12.5	41.6
Second best	15.5	51.6	6.0	20.0	8.5	28.3
Poorest	9.0	30.0	12.0	40.0	9.0	30.0
Increase in caries score						
Best	8.5	28.3	13.5	45.0	8.0	26.6
Second best	10.0	33.3	5.5	18.3	14.5	48.3
Poorest	11.5	38.3	11.0	36.6	7.5	25.0
Percentage of increase in caries score						
Best	9.0	30.0	11.0	36.6	10.0	33.3
Second best	11.0	36.6	10.0	33.3	9.0	30.0
Poorest	10.0	33.3	9.0	30.0	11.0	36.6

* Best indicates least advance in carious condition.

2.1 for the milk and 1.9 for the D milk group; the average increase in number of cavities was 6.4, 5.6 and 6.2, respectively, and the average increase in the caries score was 19.4, 18.7 and 19.8 points, respectively, for the three groups (chart 1 *A, B, C* and table 5). Since the groups started with slightly different scores, however, the percentage of advance furnishes fairer comparison. On this basis the tendency for a slightly smaller advance in carious condition by the milk groups is more pronounced (chart 1 *D, E, F*). The percentage of advance for the respective groups was 28.7, 26.2 and 21.5 for number of teeth affected; 54.5, 46 and 50.7 for number of cavities, and 107, 92.6 and 94.6 for the caries score.

In records of the individual children in the groups there was again a suggestion of a slight advantage for the children given milk (table 7). The percentage of children having 5 or more new carious teeth was 16.7 for the control group and 13.3 for both the milk groups; the per-

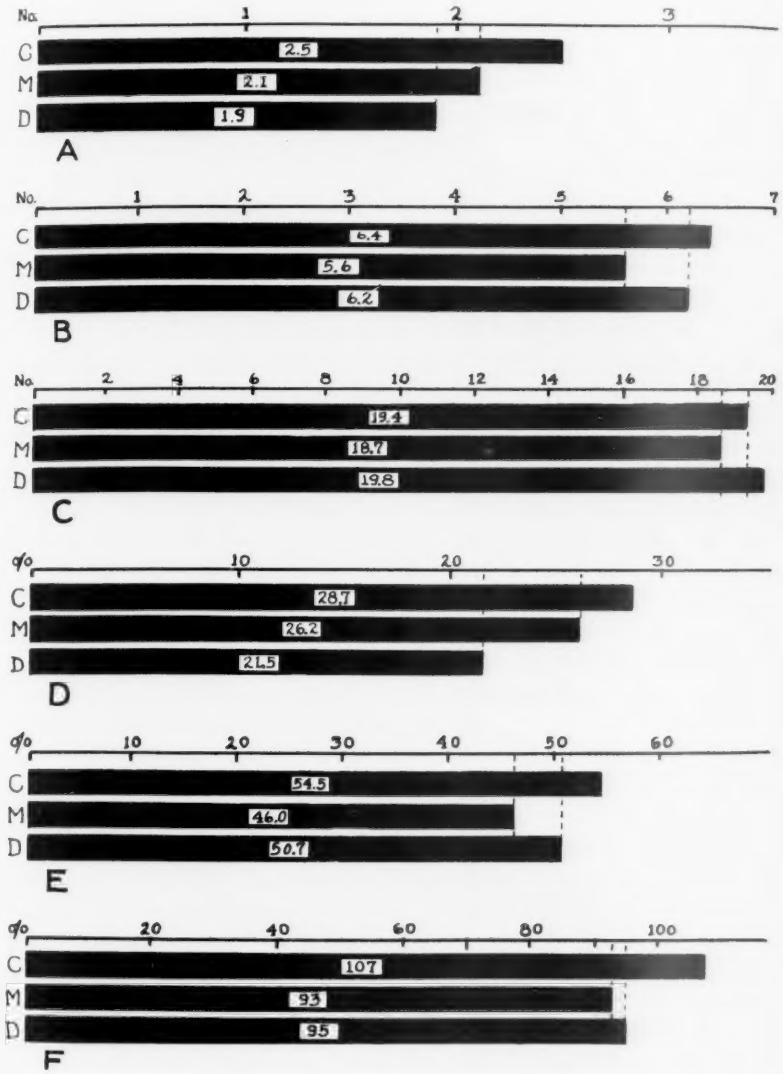

Chart 1.—Advance in carious condition for control (*C*), plain milk (*M*) and irradiated milk (*D*) groups during the year. *A* indicates mean number of newly carious teeth for each group; *B*, mean number of new cavities for each group; *C*, mean advance in the caries score; *D*, percentage of advance in number of carious teeth; *E*, percentage of advance in number of cavities; *F*, percentage of advance in the caries score.

centage of children having 10 or more new cavities was 43.3 for the control and 20 and 30 for the respective milk groups. The percentage having a total increase in the caries score of 30 points or more was 23.3 for the control, 20 for the milk and 16.7 for the D milk group.

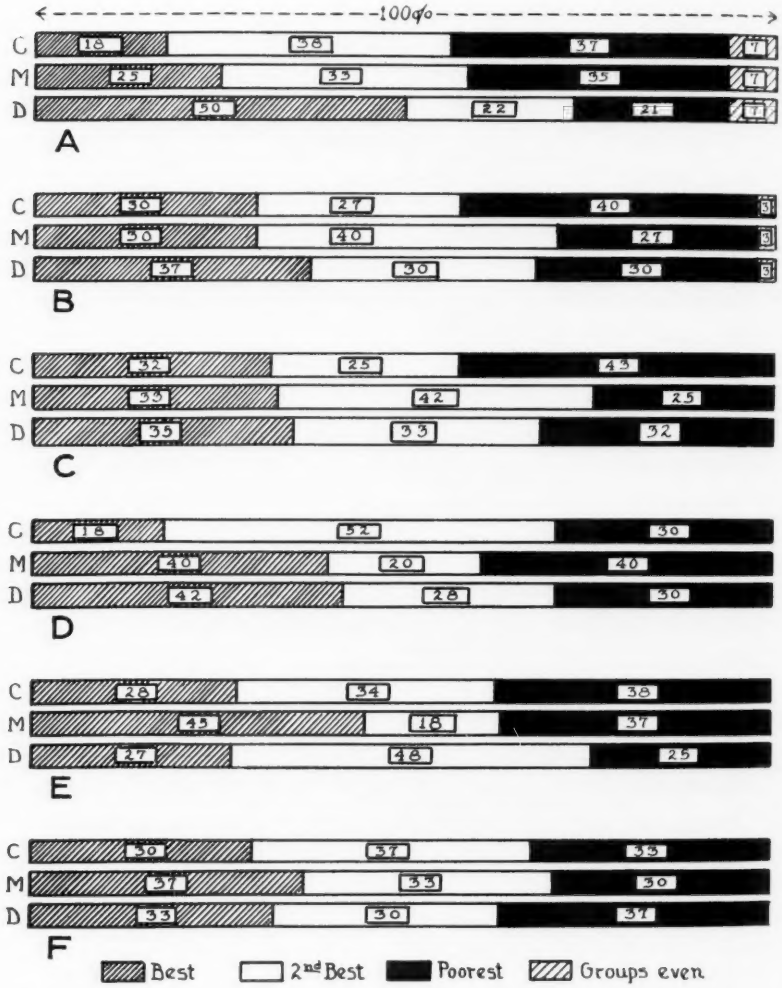

Chart 2.—Percentage of times in thirty matched trios the control (*C*), the child given plain milk (*M*) and the child given D milk (*D*) made the best, the next best and the poorest record for the year. "Best" in each case means least advance in the item specified. A favorable record is indicated by a longer hatched bar at the left and a shorter black bar at the right. *A* indicates increase in number of carious teeth; *B*, percentage of increase in number of carious teeth; *C*, increase in number of cavities; *D*, precentage of increase in number of cavities; *E*, increase in the caries score; *F*, percentage of increase in the caries score.

These differences were not large, nor were they statistically significant, but it is interesting that they tended in the direction that might be expected.

A final test that may be applied is a comparison of the progress of caries for individuals in the 30 matched trios. This is a severe test, for the 3 children in each trio were not perfectly matched, and, as earlier pointed out, other, unexplained variables would tend to obscure small differences due to the dietary supplement. Nevertheless, it was deemed of interest to compare the partners in the several groups on all possible bases, namely, (1) number of newly carious teeth, (2) percentage of increase in carious teeth, (3) number of new cavities, (4) percentage of increase in cavities, (5) increase in the caries score and (6) percentage of increase in the caries score. The values of these items for the 3 children in each trio were lined up side by side for comparison, being listed as best, second best and poorest in the trio ("best" indicating least advance in decay). The results of this tabulation was summarized in table 8 and chart 2. While there was, as in the preceding analyses, no outstanding tendency for the milk groups to excel the control group, again such differences as did exist tended in this direction. This can best be observed in the 6 graphs if it is remembered that in the hatched portions at the left a long bar represents an advantage, as it indicates a larger proportion of times the group had the best gains, while in the black portions at the extreme right a short bar means an advantage, since this indicates a smaller proportion of times the group fell to third place. If both ends of the scale are considered, there are 12 opportunities for a group to have the best record (that is, 6 comparisons in which it could have the longest hatched bar at the left and 6 in which it could have the shortest black bar at the right). It will be observed that the milk group was better than the control in 10 and the D milk in 9 of the comparisons. Both milk groups, moreover, excelled the control in 8 of their 12 opportunities. By every method of analysis, then, there was a consistent tendency for the progress of caries in the groups given a supplement to be slightly less than in the control group. The differences were, however, too small to be of either statistical or practical significance.

COMMENT

In view of the striking results reported by other workers for arrest of caries with dietary improvement, the findings in this study are disappointing. In the studies of Boyd and Drain, giving subjects an improved diet for even a few weeks resulted in an arrest of caries which was noticeable to the dentist on clinical examination. Others have reported similar striking results. Why, then, the failure to duplicate these findings in the present study? There are several possible

explanations. The first and most obvious is that even with the addition of the supplementary pint of milk, the diets were still inadequate in a number of important elements, most notably in vitamin C. This will be shown in a later report dealing with the dietary study. It is well known that vitamin C plays an important role in development of teeth and, according to some workers, in prevention of dental caries, and lack of this vitamin may well have been a limiting factor in the present study. It seems probable, moreover, as many workers have suggested, that so far as diet is concerned, dental integrity can be maintained only by a diet adequate in all essentials. This point is especially stressed by Boyd and Drain, and it is noteworthy that all the diets reported by them as having caused arrest of caries have been well fortified in all constituents. The present study also might be used to defend this theory. Another possible factor should be considered, namely, the relatively high percentage of sweets and other carbohydrates in the diets of these children. The proportion of carbohydrate was not only well above that which is usually considered desirable, but sugar in the form of cookies, jelly, sweet rolls and candy was used in appreciable amounts. Those workers, therefore, who believe in the harmful effects of an excess of sweets could find ample support for their theories in the situation here described.

In any case it is evident that, whatever the factor or factors responsible for the extreme degree of caries in this institution, they were modified only slightly by addition of the pint of milk either with or without vitamin D. This does not necessarily mean that either milk or extra vitamin D was not needed; it may mean merely that the favorable effects of these were offset by limitations of the diet or by other unfavorable factors. The possible reasons for the failure to find any significant effect of the vitamin D given in the irradiated milk have been discussed in the previous report, which deals with ossification of the carpal bones. Briefly, the explanation would appear to be either (1) that the children were already receiving all the vitamin D needed or (2) that the 70 units supplied was not enough to produce measurable results under the conditions of the experiment.

The significant observation regarding the entire investigation, as reported in this article and in the two preceding ones, is that the results of all three studies are uniformly consistent. This is shown most clearly by the three sets of charts showing the year's changes in the several aspects of development. By every method of comparison, the children given a milk supplement are found to have an advantage over the controls. They made better growth in height and weight and more progress in development of bone, as judged by ossification of the bones of the wrist; and, as shown in the present study, there was a slight

tendency toward retardation of the rate of dental decay. Taken together these studies clearly indicate that the additional milk supplemented some, though not all, of the deficiencies in the rather mediocre institutional diet and proved to that extent a factor of safety.

In the light of these findings, it is to be regretted that the study could not be continued for another year, with all the deficiencies in the diets supplemented in order to determine whether a diet fully adequate in every way would be effective in arresting the extremely progressive caries in this institution.

SUMMARY

The effect of a milk supplement, with and without added vitamin D, on the development and spread of dental caries was observed for 90 children in an institution over a calendar year. The children were divided into three groups, matched as closely as possible on the basis of age, sex and degree of caries. One group remained as controls; the other two received daily per child a pint equivalent of evaporated milk, one having it in irradiated and the other in nonirradiated form.

All the children showed extremely progressive caries. For the entire group there was a 26 per cent advance in number of carious teeth, a 50 per cent advance in number of cavities and a 98 per cent advance in the caries score.

Although the difference in advance in caries between the groups was small and statistically insignificant, there was a consistent tendency according to all methods of comparison for the progress of caries to be slightly less for the children given a supplement than for the control children, with no consistent difference between the two groups given different types of milk. The percentage of increase in carious teeth was 28.7 for the control, 26.2 for the milk and 21.5 for the D milk group. The corresponding percentage of increase in number of cavities was 54.6, 46 and 50.7, and the increase in score 107, 92.6 and 94.6, respectively for the three groups. These results indicate that the supplement tended to inhibit the rate of dental decay but that other factors also were involved.

Dr. W. I. Williams and Dr. R. Kronfeld gave counsel and assistance during the course of the study, and the Ritter Dental Equipment Company loaned the roentgen apparatus.

Case Reports

POSTVACCINAL ENCEPHALOMYELITIS

STANLEY S. LAMM, M.D.
BROOKLYN

Approximately 75 cases of encephalomyelitis which followed vaccination against smallpox have been reported in the United States, with a mortality of about 40 per cent. The disease has generally followed a primary inoculation, although in two reported instances it has occurred after a second.[1] In the majority of cases in which encephalomyelitis has developed, vaccination has been performed on patients of school age. In an instance reported in the Netherlands,[2] a 13 year old child died four days after vaccination. At the time of death there was no "take" at the site of vaccination; however, autopsy revealed the presence of lesions of the central nervous system similar to those of postvaccinal encephalitis.

The incubation period of postvaccinal encephalomyelitis ranges from seven to twelve days, and the disease is ushered in with acute manifestations. Characteristically there are headache, vomiting, drowsiness, fever, stiffness of the neck and paralysis. Zappert [3] has described six clinical forms: namely, meningeal; somnolent-paretic, which simulates epidemic encephalitis and may be accompanied by paralysis of the extremities, disturbance of the bladder and paralysis of the ocular muscles; convulsive; trismic; neuritic, and myelitic. The local lesion of a patient in whom encephalitis develops is in no way different from the ordinary "vaccination sore." The spinal fluid may show a slight cellular increase, as a rule with lymphocytic predominance. The fluid is sterile.

The duration of the disease is from two to three weeks. When recovery occurs it is usually complete and without sequelae. Following is the report of my case with the postmortem observations.

REPORT OF A CASE

D. M., a white girl 5 years of age, was admitted to the Long Island College Hospital on Oct. 8, 1936, because of pain in the left leg and inability to move it, drowsiness and fever of twenty-four hours' duration.

From the Department of Pediatrics and the Department of Pathology of the Long Island College of Medicine and the Long Island College Hospital.

1. Armstrong, C.: Pub. Health Rep. **47**:1553, 1932.
2. Querido, A., cited by Newman, S.: J. Pediat. **3**:461, 1933.
3. Zappert, cited by de Crinis, M.: Frankfurt. Ztschr. f. Path. **48**:474, 1935.

On September 15 an attempt to vaccinate the child on the left arm had been made without success. On September 30 the attempt had been repeated. A "vaccination sore" developed at the site. At first the child continued to attend school regularly, but one week after vaccination she left her playmates suddenly and went home feeling ill, drowsy and with a fever. That evening she complained of pain in the left leg, and by the following morning was unable to move it. There were persistent pain, headache, fever and increasing drowsiness.

The family history was irrelevant. The birth of the child was normal, and her development was satisfactory except for a certain degree of undernutrition. The past diseases of interest were pneumonia in infancy, and measles, followed by pertussis at the age of 3. There had been no complications or sequelae.

Examination.—The temperature of the patient on admission was 102.2 F., the pulse rate was 110 and the respiratory rate 26. Diffuse erythema was present on the chest, the abdomen and the small of the back. There were marked rigidity of the neck and stiffness of the spine in the dorsal and the lumbar regions. The child was drowsy and became irritable when attempts were made to arouse her. She made no attempt to move the left leg, and passive motion caused apparent pain. The left lower extremity was paralyzed and all reflexes were absent. The right lower extremity was normal in its movements and reflexes. There was no clonus or Babinski reflex. The upper extremities and the intercostal muscles were normal. The muscles of the abdominal wall on the left side bulged on coughing but the right side of the abdomen was partially paretic. The abdominal reflexes were absent. Facial palsy was present on the right side. The left eyelid was ptosed. The extraocular movements were normal; the pupils were regular and equal and reacted to light; there was no nystagmus, and the fundi were normal. The tongue did not deviate and moved normally, as did the soft palate. Hearing and vision seemed unaffected. On the left arm was a typical "vaccination sore." There were no enlarged axillary glands, no masses in the abdomen and no pathologic condition of the ears, the heart or the lungs. The throat was slightly injected.

Lumbar puncture revealed a clear spinal fluid under normal pressure and containing five hundred cells. Of these, 94 per cent were polymorphonuclear. The sugar content was 66 mg. per hundred cubic centimeters; the reaction to the Pandy test was 2 plus. No organisms were found on direct smear. The culture of the spinal fluid was sterile. Successive samples appeared similar, with cell counts which gradually decreased to normal. The sugar content of the spinal fluid remained normal. Further cultures and smears revealed no organisms. Blood cultures were sterile. The Mantoux reaction and the reactions to Wassermann tests of both blood and spinal fluid were negative. The culture of the throat contained Micrococcus catarrhalis and Streptococcus haemolyticus in small numbers; the nasal culture showed Staphylococcus aureus, and the culture of the urine, Bacillus coli.

Course.—The day after admission the patient became worse, with the development of hyperthermia (108 F.) and with a pulse rate ranging from 140 to 170. Left internal strabismus was present. Respirations were shallow and intermittently irregular, with intervening periods of apnea. The upper extremities at first became athetotic; later they became rigid and fixed in an extended position, though reflexes were still present. In both lower extremities there was flaccid paralysis with absence of reflexes. The bladder was distended.

Treatment was symptomatic and consisted of lumbar punctures, of intravenous injections of hypertonic dextrose and of blood transfusions. The bladder was regularly catheterized.

Fig. 1.—Cellular infiltration in the Virchow-Robin sheaths of several small vessels in the pons. The tissue about them stains poorly and is fragmented and edematous. Magnification, 200.

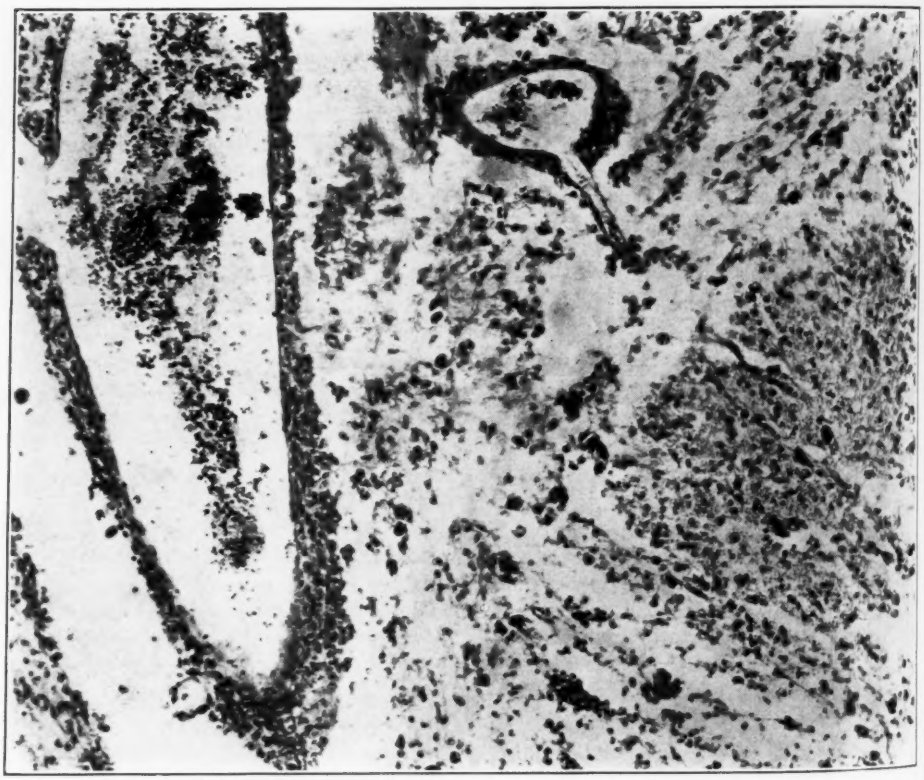

Fig. 2.—Extreme softening and disintegration of the neural tissue about a larger vessel in the pons. The larger dark cells in the center of the figure are persisting ganglion cells. Magnification, 200.

The patient entered a deep coma. The right pupil was dilated and rotated upward. Diaphragmatic activity seemed absent, there being an overactivity of the intercostal muscles and the accessory muscles of inspiration. Bronchopneumonia developed, and the patient died on October 21, two weeks after onset of the symptoms.

The clinical history and course indicated postvaccinal encephalomyelitis, with particular involvement of the brain stem and the spinal cord.

Postmortem Observations (Dr. K. Strong).—The necropsy was performed ten hours after death. The general examination revealed a crusted lesion of the

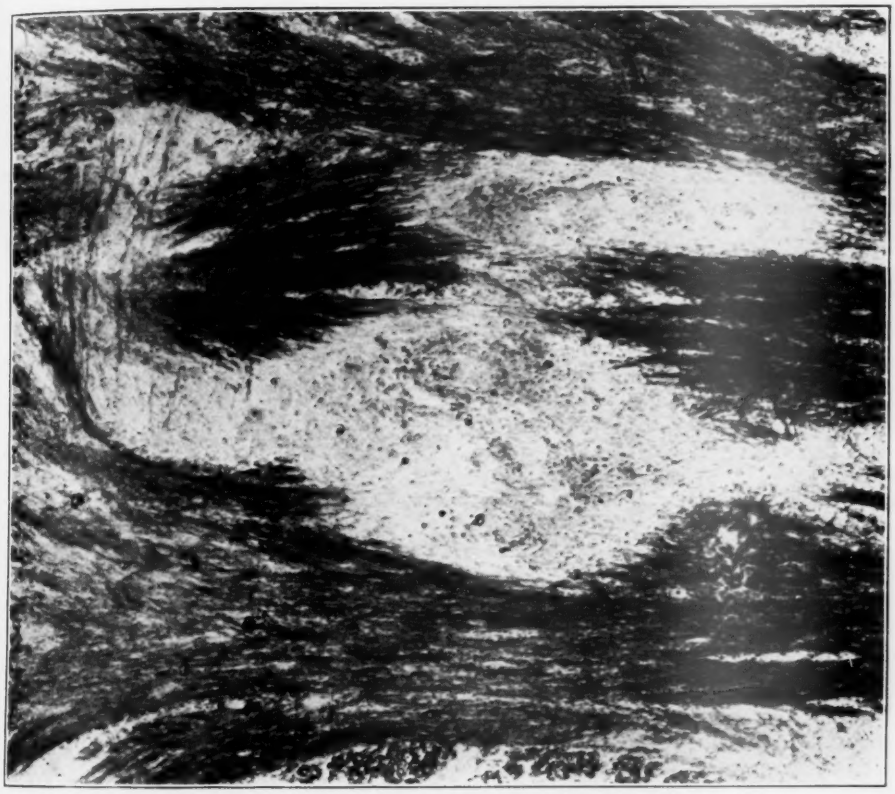

Fig. 3.—Spielmeyer stain showing demyelination of medullated fibers in the pons. In the center of the field the lumen of a small vessel is seen. The originally continuous transverse band of black-stained medullated fibers is interrupted in the area about the vessel. Magnification, 200.

skin in the region of the left deltoid, involution of the thymus, moderate dilatation of the heart, extensive bronchopneumonia, acute pyelonephritis and acute cystitis. A culture of blood from the heart was negative. Cultures from the bladder and the kidneys yielded an enterococcus overgrown by Bacillus pyocyaneus.

Examination of the nervous system showed that the vessels of the brain were congested and that in the rostral portion of the pons was an ellipsoid mass (15 by 10 mm.) of reddish gray, slightly softened tissue. A portion of the upper cervical cord and a segment of the lumbar cord were removed.

On microscopic examination of the brain the most extensive lesion was found in the pons (figs. 1 and 2), where there were large areas of poorly staining, fragmented, edematous tissue having about them similar smaller, isolated foci, often in a perivascular position. In these areas of tissue ganglion cells persisted, and there were several minute hemorrhages and numerous large phagocytic cells with foamy cytoplasm. Similar phagocytic cells were the chief components of prominent cellular aggregates about a number of the vessels. The neural tissue and the meninges were free from leukocytic infiltration.

In Spielmeyer (fig. 3) and Pal-Weigert preparations extensive demyelination was evident, and the smaller lesions were perivascular. The cytoplasm of the

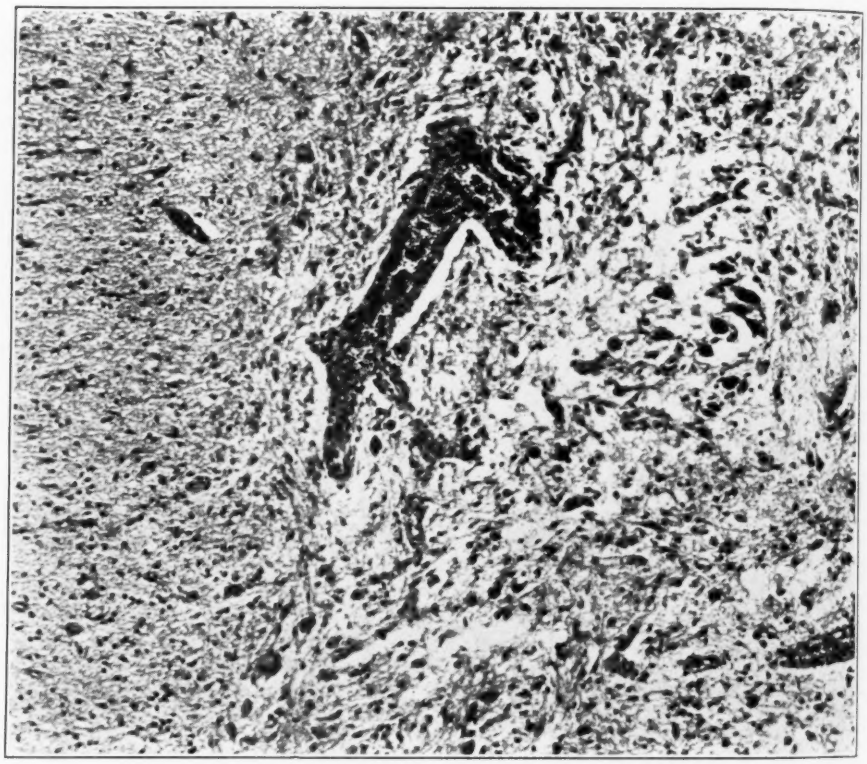

Fig. 4.—Cellular infiltration and extensive disintegration of the gray substance about a vessel in the lumbar portion of the cord. Note the persisting ganglion cells to the right of the vessel. To the left of the vessel the white substance of the cord is well preserved. Magnification, 200.

large phagocytic cells which occurred in the areas of demyelination and about the vessels stained deeply with sudan III. In the eosin–methylene blue stain there was evident a variable lysis of the Nissl substance of the ganglion cells in the areas of demyelination. Some of these cells were well preserved. In the Giemsa and Gram stain preparations bacteria were not found. In the medulla, cerebellum and lumbar cord (fig. 4) were smaller areas of defective staining of edema and of fragmentation which were likewise characterized by perivascular

demyelination (fig. 5), by persistence of ganglion cells and by lack of leukocyte infiltration.

The cerebral cortex, the internal capsule, the basal ganglions, the thalamus and the mesencephalon revealed an occasional inconspicuous focus of perivascular demyelination. Sections of the hypophysis and of the pineal body showed no abnormal condition. In the upper cervical cord a few phagocytic cells were present about vessels, but there was no loss of myelin. Save for the presence of a few small round cells in the leptomeninges of the lumbar portion of the cord, in all sections the meninges were free from cellular infiltration. The mid-thoracic portion of the left phrenic nerve showed extensive demyelination.

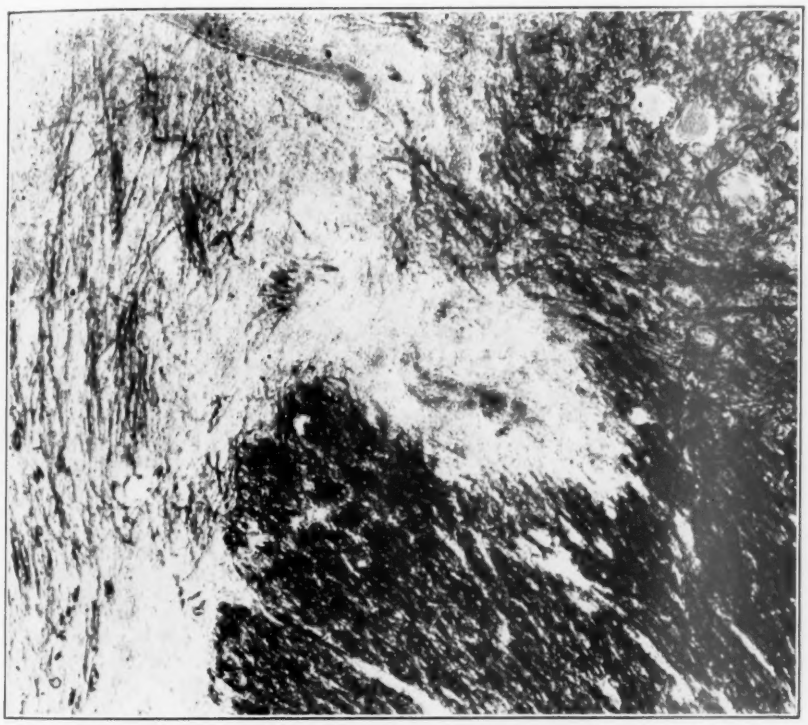

Fig. 5.—Pal-Weigert stain showing demyelination about a small vessel in the white substance of the lumbar portion of the cord.

COMMENT

The pathologic conditions seen in this case are in accordance with the descriptions of postvaccinal encephalitis by Turnbull and McIntosh,[4] Perdrau [5] and Flexner.[6] The process is essentially a diffuse encephalomyelitis which particularly involves the brain stem and the cord. Gen-

4. Turnbull, H. M., and McIntosh, J.: Brit. J. Exper. Path. **7**:181, 1926.

5. Perdrau, J. R.: J. Path. & Bact. **31**:17, 1928.

6. Flexner, S.: Postvaccinal Encephalitis and Allied Conditions, J. A. M. A. **94**:305 (Feb. 1) 1930.

erally, the cerebral cortex is spared. Both the white and the gray matter are affected, but the white is especially so. The lesion is degenerative and leads to areas of softening and demyelination in which there are perivascular infiltration and vascular engorgement. About these areas many cells accumulate. The cellular infiltrations are both adventitial and periadventitial. With respect to the extent of involvement, the cord is just as important as the brain. The ganglionic cells participate but little. There is microglial proliferation with phagocytosis of the broken-down myelin.

The cause of the condition is undetermined. The most widely accepted theory at present is that encephalomyelitis is due either to activation of a latent neurotropic virus or to production of the disease by the virus of smallpox itself.[7] The vaccine virus has occasionally been recovered from the spinal fluid.[1] Experimentation with animals to produce postvaccinal encephalitis has failed.[7] Attempts have been made to treat the disease by intraspinal and intravenous injection of the serum of persons recently vaccinated, but the conclusions reached as to the efficacy of this treatment are indefinite.[7] At the present time it seems that vaccinal encephalomyelitis may best be avoided by vaccinating during the first year of life. Furthermore, since Armstrong [1] has shown in mice that previous inoculation with diphtheria toxoid renders the organism more resistant to vaccine virus, it seems preferable first to immunize infants against diphtheria. This measure would develop virus antibodies and a general immunity which would protect them against the vaccine virus when it is introduced at a later date.

225 Eastern Parkway.

7. Report of Encephalitis Committee in Holland, Am. J. Dis. Child. **44**:186 (July) 1932.

MULTIPLE CYSTIC TUBERCULOSIS OF THE BONES IN CHILDREN

JOHN L. LAW, M.D.

AND

W. S. PERHAM, M.D.

ANN ARBOR, MICH.

Three factors probably predicate the rarity of cystic tuberculosis of the diaphysis of long bones. After an infection of the blood stream, localization of the tubercle bacillus in the bones elects the metaphyses owing to the anatomic situation of the end arteries; the caseous process of a tuberculous lesion of a bone is usually more rapid than fibrosis and may lead to abscess or sinus formation; generalized tuberculous infections in children are apt to precipitate a fatal outcome in a relatively short time.

The report of Jüngling [1] in 1920 of a tuberculous cystic condition of bones drew attention to an uncommon pathologic type which he termed osteitis tuberculosa multiplex cystica. In Jüngling's second report [2] 55 cases of this condition were reviewed, including 9 cases of his own. The characteristic features of the disease were listed as follows:

1. The onset was gradual with or without moderate pain in the involved part and unaccompanied by fever or by much general disability.

2. The onset usually occurred during puberty or between the ages of 20 and 30, the two sexes being equally affected. The disease in its typical form in children was not recorded.

3. The disease involved the small long bones of the hands and feet, exceptionally the long hollow bones. Jüngling stated, "The disease is rarely to be seen affecting other bones than the metacarpals, metatarsals, and phalanges, so that there is nothing particular to be observed in this connection, yet even here the change appears to consist in purely circumscribed light spots without perifocal reaction." In his report, however, there were 7 cases in which bones other than the small long bones of the hands and feet were involved: nasal bones, 4 cases; tibia, 1; ulna, 1, and femur and humerus, 1.

From the Department of Pediatrics and the Department of Surgery of the Medical School of the University of Michigan.

1. Jüngling, O.: Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:375, 1920.

2. Jüngling, O.: Beitr. z. klin. Chir. **143**:401, 1928.

4. The disease was associated with lesions of the skin, which in their order of occurrence were lupus pernio, Boeck's sarcoid, lupus vulgaris, lupus exfoliativus, erythema induratum of Bazin and scrofuloderma.

5. A tendency to vary in form, which was demonstrable by roentgenogram, was shown. The fundamental picture consisted of circumscribed

TABLE 1.—*Summary of Reported Cases*

Author	Year	Age	Duration of Disease	Local Symptoms and Signs	Site of Lesions
1. Vastine, J. H., and Bacon, E. P.	1935	17 mo.	11 mo. when first examined	"Lumps" on fingers, wrist, ankle and foot for 11 mo.	Metacarpals, metatarsals, phalanges, lower end of ulna, external malleolus, skull, left sixth rib, mandible, right femur, right tibia, right fibula
2. Idem	1935	2 yr.	1 mo. when first examined	Swelling of left hand for 1 mo.	Mandible, metatarsals
3. Schwentker, F. F.	1931	1 yr.	Questionable	Swelling of left elbow and leg	Ulna, left fibula
4. Jacobsen, A. W.	March 1936	8 yr.	7 yr.	No complaints referable to the osseous lesions	Humeri, ulnas, tibias, metacarpals, phalanges, metatarsals, left radius
5. Petter, C. K., and Medelman, J. P.	1935	10 mo.	4 mo.	No symptoms	Right humerus
6. Denks, H.	1933	8 yr.	3 yr.	Painful swelling of right hand	Bones of hand, left second metacarpal, left humerus, right femur
7. Acuña, M.; Puglisi, A., and Vallino, M. T.	1933	19 mo.	7 mo.	Swelling of arm and leg, and pain on pressure	Right ulna, right tibia, phalanges of right hand
8. Idem	1933	2½ yr.	1 yr.	Pain and swelling of right elbow	Right humerus, right radius
9. Stalmann, A.	1934	1½ yr.	6-8 mo.	Swelling of fingers, red-blue discoloration of skin of fingers over lesions; no pain	Phalanges of both hands
10. Bayer, W.	1933	9 yr.	2 mo. (4½ yr.)	Swelling of fingers; some limitation of motion; some redness of skin (Boeck's sarcoid); no pain	Phalanges of both hands and of both feet

"honeycombed" areas of rarefaction without sclerosing reaction around them; there was no periostitis and no sequestration.

6. A tuberculin test usually gave negative results, as did inoculation of a guinea pig.

7. Involved areas of bone showed no caseation but were filled with granulation tissue composed of epithelial cells, fibroblasts, lymphocytes and, in rare instances, giant cells. No tubercle bacilli were found on section.

8. The cystic "honeycombed" areas of rarefaction either remained stationary in appearance, retrogressed, healed slowly or healed completely.

Contrary to Jüngling's expressed opinion that osteitis tuberculosa multiplex cystica probably never occurs in its typical form in children, the literature records at least 7 cases [3] of this chronic special form of tuberculosis of the bone in which the small bones of the hands or feet were involved (table 1). Contrary also to Jüngling's observation that the disease rarely affected the long hollow bones, the literature records 3

ultiple Cystic Tuberculosis in Children

Proved by Basis of Diagnosis	Treatment	Results	Comment
ntracutaneous tuberculin est —; biopsy revealed ypical tubercles of bone; oentgenogram of bones ypical	General treatment; conservative treatment for tuberculosis	Improvement of osseous lesions; death from bronchopneumonia at age of 3½	Roentgenogram of chest showed hilar adenopathy and childhood tuberculosis
ntracutaneous tuberculin est —; roentgenogram of ones typical	General treatment; conservative treatment for tuberculosis	Little change in osseous lesions	Roentgenogram of chest showed hilar adenopathy and thickened pleura
uberculin test +; roentenogram of bones typical; noculation of guinea pig +	General care; antisyphilitic treatment (Wassermann reaction was +)	Almost complete healing of osseous lesions	Roentgenogram of chest showed enlarged tracheobronchial glands
ntracutaneous tuberculin est —; roentgenogram of ones typical; inoculation f guinea pig —	General care; desensitization to tuberculin	Improvement in osseous lesions; death from miliary tuberculosis and tuberculous peritonitis at age of 13	Roentgenogram of chest showed hilar adenopathy; autopsy revealed spread of tubercles to all organs; tuberculous peritonitis
oentgenogram of bones +	Symptomatic treatment; sanatorium care	Gradual improvement of osseous lesion	Roentgenogram of chest showed primary pulmonary tuberculosis
oentgenogram of bones ypical; tuberculin test +	Sanatorium care	Left humerus healed in 3 yr.; hand healed in 1½ yr.; femur healed in 1½ yr.	Roentgenogram of chest showed calcified hilar glands
Mantoux tuberculin reacon 3+; roentgenogram of one typical; inoculation of ervical gland of guinea pig + for tuberculosis, microcopic tubercles of skin over and; biopsy of bone —	General care; local subcutaneous injections of "Gadusan" over tuberculous site	Temporary progression and regression of osseous lesions; death from general tuberculosis 1 mo. after first examination	Fistulous opening at site of lesion at right ulna; roentgenogram of chest —
Mantoux reaction 3+; oentgenogram of bones ypical	Seashore vacation; general care; iodides; ultraviolet ray; liver extract	Some improvement of osseous lesions; general health improved	Fistulous opening at site of both lesions; roentgenogram of chest —
irquet reaction —; inocula- on of guinea pig +; inical examination +; oentgenogram of bones ypical	General care	Lesions stationary after 3 mo.	No statement
ntracutaneous tuberculin est —; inoculation of uinea pig —; roentgenogic appearance typical; inical examination +	General care; seashore vacation; numerous drugs	Moderate improvement of osseous lesions	Roentgenogram of chest showed hilar adenopathy

cases [4] in which the process was confined to the long hollow bones (table 1). It is seen from table 1 that involvement of the long hollow bones is predominant in these children.

3. (*a*) Vastine, J. H., and Bacon, E. P.: Radiology **24**:22, 1935. (*b*) Jacobsen, A. W.: J. Pediat. **8**:292, 1936. (*c*) Denks, H.: Fortschr. a. d. Geb. d. Röntgenstrahlen **48**:584, 1933. (*d*) Acuña, M.; Puglisi, A., and Vallino, M. T.: Arch. argent. de pediat. **4**:268, 1933. (*e*) Stalmann, A.: Arch. f. klin. Chir. **178**:669, 1934. (*f*) Bayer, W.: Jahrb. f. Kinderh. **138**:31, 1933.

4. (*a*) Schwentker, F. F.: Cystic Tuberculosis of the Bone, Am. J. Dis. Child. **42**:102 (July) 1931. (*b*) Petter, C. K., and Medelman, J. P.: Am. Rev. Tuberc. **32**:285, 1935. (*c*) Denks.[3c]

Recently we have had the opportunity of studying a child with multiple cystic tuberculosis of the shafts of the long bones for two years. The history and the clinical and laboratory observations are as follows:

REPORT OF A CASE

A girl aged 6 years was admitted to the University Hospital in the pediatric service March 25, 1935, with the complaint that since June 1934 she had been failing in health, mainly evidenced by ease of fatigue, by poor appetite, by fever at night and by a slight deformity of the back of four months' duration.

Family History.—Both parents and five other children were living and well. One child had died of brain fever two years before, at the age of 21 months (details of illness not ascertainable). There had been no tuberculosis in the family and no known tuberculous contact. The family supply of milk was obtained from tuberculin-tested cattle and was pasteurized.

The home conditions were satisfactory, the diet ample and the patient's habits regular.

Past History.—The patient was born on April 30, 1928, at full term and normally. Her weight at birth was 7 pounds (3,175 Gm.), and her state of health was good during the first few weeks. She was breast fed for two months and then received modified cow's milk and oatmeal water at regular intervals and was given orange juice and cod liver oil daily. Development was normal; the first teeth erupted at 7 months; sitting erect began at 9 months, walking at 14 months and talking at about that age.

Previous diseases included chickenpox in 1932, bronchitis in the same year and measles the following year. She had not been vaccinated or immunized against diphtheria. Except for the illnesses mentioned, the general health was good up to the time the child was 4 years old, when, it is said, she slowed up, would not play and seemed dull and apathetic, especially in the evening, though she was brighter in the morning.

Present Illness.—In June 1934 the child's mother noticed that she had worms. Treatment was prescribed, but after this she did not gain strength and there was considerable malaise. During the summer she had fever nearly every night, and her hair began to fall out. By September her general condition had improved and she started to school, but she was so fatigued by late afternoon that it was thought advisable to keep her at home to rest. In November her physician noted a kyphotic deformity of the spine; he took a roentgenogram, diagnosed the condition as tuberculosis and on Dec. 14 applied a body cast. When the cast was bivalved three months later and no improvement was apparent, the patient was sent to the University Hospital.

Examination.—On admission the patient was well nourished and developed and did not appear acutely ill. Her height was 44½ inches (112 cm.) and her weight 37¼ pounds (16.9 Kg.). Results of a general physical examination were negative, except for a slight exaggeration of the reflexes of the lower extremities and for the condition of the back. There was kyphosis in the midthoracic region, with definite protuberance of three vertebrae and some tenderness to pressure. An intracutaneous test with tuberculin in a 1:50,000 dilution gave negative results. A 1 to 1,000 dilution elicited a 2 plus reaction. Roentgenograms of the spine and

of the chest demonstrated a destructive process involving the bodies of the seventh, eighth, and ninth thoracic vertebrae. The eighth dorsal body was almost completely destroyed. There was a definite angulation and the beginning of an early kyphos formation. An anteroposterior roentgenogram showed a list to the right at this level, with a mass of soft tissue around the spine, representing a paravertebral abscess. The intervertebral disk between the eighth and the ninth vertebra was lost. Roentgenograms of the chest showed gross tuberculous adenopathy, peritracheal without parenchymal lesion (figs. 1 and 2).

Incident to the first roentgenographic examination of the chest, gross changes in both scapulas were demonstrated, giving the appearance of a destructive lesion involving the scapular body and the base of the scapular spine. The acromion process also seemed to be involved. The distal end of the left humerus showed localized changes within the shaft, new subperiosteal bone with elevation of the periosteum (fig. 3). Detection of these changes in bone led to roentgenographic examination of the skull and the long bones, and numerous abnormalities of bone were revealed.

Destructive lesions were noted in both scapulas, in the right and left clavicles, in the skull, in the left humerus and the left radius, in the right humerus and the right radius, in the first, fourth, fifth, sixth and ninth left ribs, in the left iliac bone, in the third and fifth lumbar vertebrae, in the right and left tibias and in the left fibula (table 2).

Diagnoses entertained besides tuberculosis were hyperparathyroidism, multiple myeloma, and atypical Schüller-Christian disease. The results of the routine laboratory studies, including urinalysis and a blood count, were negative. The Kahn test was negative. Additional tests showed the calcium content of the blood to be 11.5 mg. per hundred cubic centimeters; the phosphorus content, 4.1 mg.; the cholesterol content, 221 mg.; the total lipid content, 492 mg., and the sugar content (fasting) 71 mg. A second urinalysis did not show the presence of Bence Jones protein.

In view of the positive reaction to the tuberculin test, the obvious tuberculous lesion of the thoracic spine, the presumptive gross tuberculous hilar adenopathy, the normal urine, the unchanged blood chemistry, the absence of any sign of xanthoma and the local roentgen appearances, it was felt that the widely disseminated skeletal lesions were quiescent tuberculous processes. Treatment with a Bradford frame and general supportive dietetic and hygienic measures were instituted on April 9, two weeks after the child's admission to the hospital.

Course.—During the first month in the hospital, the patient contracted an infection of the respiratory tract and otitis media developed; this subsided without myringotomy. To substantiate further the diagnosis of tuberculosis of the long bones, a biopsy of the lesion of the right scapula was performed May 15. Purulent material was encountered, but cultures of the pus proved negative. (By error, staining and culture for tubercle bacilli and inoculation of a guinea pig were not done.) The pathologic report of the biopsy was "active chronic tuberculous osteomyelitis and osteochrondritis—extension to synovial membrane" (shoulder joint). No tubercle bacilli were found on section.

During the next two and one-half months of hospitalization, the patient's general condition improved and her weight increased 2 pounds (0.9 Kg.). Roentgen plates of the chest taken at intervals showed diminution of the hilar adenopathy, the picture approaching the normal limits (fig. 4). There was regression of the multiple lesions of the bones except in the spine, where they showed little change (table 2). On July 3 a body cast was applied for additional stabilization, and two weeks later the patient was discharged with directions for diet and with

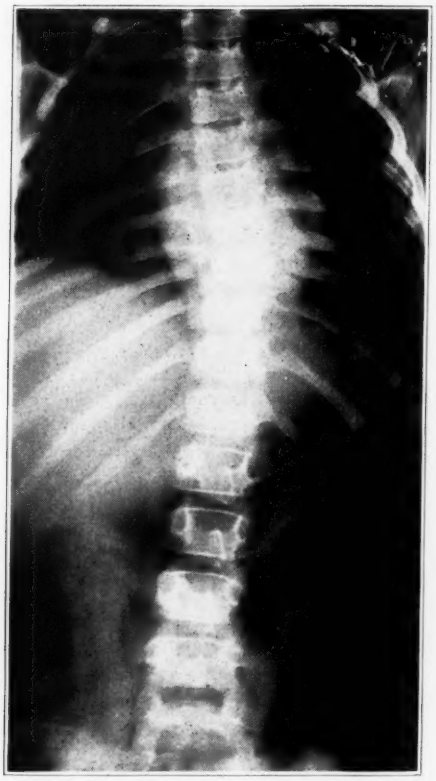

Fig. 1.—Roentgenogram taken at the time of the patient's first admission, showing dorsal Pott's disease with destruction of the dorsal bodies of the seventh, eighth and ninth thoracic vertebrae and an associated paravertebral abscess.

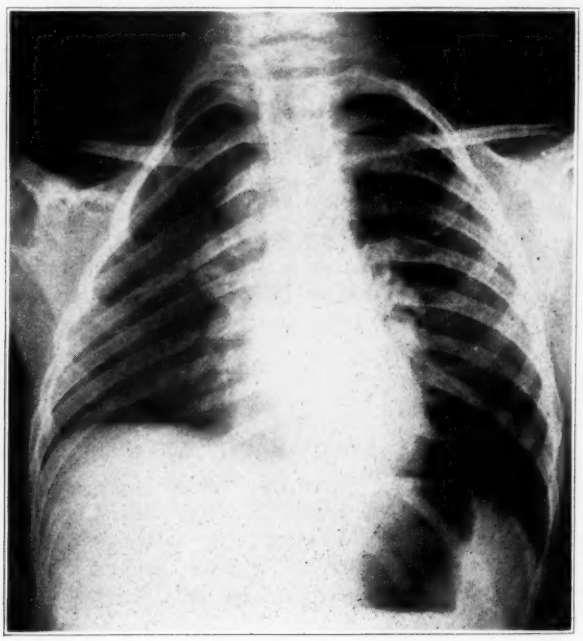

Fig. 2.—Gross tuberculous hilar adenopathy, most pronounced on the right side. There is no positive parenchymal focus.

a Bradford frame for use at home. During the next three months her condition apparently remained satisfactory. On October 14 she returned to the hospital for checkup. In December, because of advance in the spinal tuberculous process, a spinal fusion according to Hibbs's technic was performed. The fusion extended from the third to the tenth dorsal vertebra. Except for moderate postoperative surgical shock, convalescence was uneventful. Roentgenographic examination of the chest on Feb. 6, 1936, showed complete regression of the hilar adenopathy. As roentgenograms of the bones two months later showed no advance in the chronic tuberculous processes, the patient was discharged and sent home on frames.

Fig. 3.—Roentgenograms showing the condition of the left humerus at the time of the patient's admission. There are an irregular rarefied area at the distal diaphysial end, subperiosteal elevation of the bone at the medial volar surface, localized rarefaction in the medial epicondyle and an excavated area at the proximal diaphysial end of the left radius.

On examination at the time of the fourth admission, August 18, the patient was well nourished, having gained 18 pounds (4.5 Kg.) in one year. Her general condition was satisfactory and, as previously, there was no fever. Roentgenograms demonstrated further advance of the spinal tuberculosis, with collapse of the ninth dorsal vertebra; and increased destruction in the head of the right humerus at the epiphysial line. The other lesions were improved or arrested (fig. 5). The

TABLE 2.—*Roentgenographic Regression and Progression of Lesions in a Case of Multiple Cystic Tuberculosis*

Site of Lesion	Roentgenogram								
	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8	No. 9
Spine	3/27/35 Dorsal Pott's disease with destruction of the dorsal bodies of the 7th, 8th and 9th vertebrae	6/8/35 Increased destruction of the 7th and 8th dorsal bodies	11/11/35 Further advance in destruction of the 7th and 9th dorsal vertebrae	4/10/36 No change in appearance	8/27/36 Further advance in Pott's disease with almost complete destruction of 9th dorsal vertebrae	12/7/36 No change in in appearance	3/15/37 No change		
	A circumscribed rarified lesion in the medial anterior margin of the 3d and 5th lumbar bodies with sclerotic borders	Diminution of rarefaction with evidence of healing	.....	Complete disappearance of the lesions					
Lungs	3/26/35 Gross tuberculous adenopathy, peribronchial and peritracheal; no parenchymal focus	6/8/35 Tuberculous adenopathy almost completely disappeared	10/11/35 Moderate accentuation of hilar shadow bilaterally	2/6/36 Chest normal	4/10/36 No change	3/25/37 No change	6/5/37 No change		
Clavicles	3/26/27 Circumscribed area of rarefaction in the lateral tip of the right clavicle and in the median third of the left clavicle	6/8/35 Repair of rarefied areas in both clavicles	9/11/35 Both lesions completely healed	12/7/36 Normal	3/25/37 No change	6/5/37 No change			
Right scapula	3/28/35 Rarefaction and change in architectural structure of the body and supraspinatus part of the right scapula; destructive lesion in the region of the glenoid process; circumscribed area of rarefaction in the distal third of acromion process	6/8/35 Definite improvement of all lesions	10/11/35 No change except in the acromion lesion which has completely healed	4/10/36 Slight advance in destructive process in the glenoid of right scapula	8/27/36 No change	12/7/36 Destructive areas in glenoid fossa show no change	3/15/37 Advance in process involving glenoid fossa	3/25/37 No change	6/5/37 No change
Left scapula	3/28/35 Irregular circumscribed rarefied area in the superior angle of the scapula; similar lesion in the distal third of acromion process	6/8/35 Regression of lesions	10/11/35 Further regression of lesions	2/6/36 Complete healing of lesions					

	scapula; similar lesion in the distal third of acromion process							
Upper part of right extremity	3/28/35 Irregular area of rarefaction at the distal diaphysial end of the humerus (forearm not included in roentgenogram)	6/8/35 Lesion in humerus almost completely healed; circumscribed rarefaction about which there is increased density at the distal diaphysial end of the right radius	10/11/35 Complete healing of lesion in humerus; diminution in size of radial lesion	4/10/36 Further diminution in size of lesion in radius; new lesion similar in character involving lateral superior aspect of humerus on each side of epiphysial line	12/9/36 Slight residual architectural change in radius; no change in distal end of humerus; slight progression of lesion in head of humerus	3/15/37 Distal end of humerus and radius normal; no change in head of humerus	3/25/37 No change	6/5/37 No change
Upper part of left extremity	3/28/35 Irregular area of rarefaction at the distal end of humerus; subperiosteal new bone distal medial epicondyle; small round excavated area at the proximal diaphysis of the radius	6/8/35 Moderate repair of lesions in humerus and radius	10/11/35 Further slight repair of lesions	4/10/36 Lesions in humerus and radius completely cleared	12/7/36 Normal	3/15/37 Normal	3/27/36 Normal	
Skull	3/28/35 Two small circumscribed rarefied lesions located at the reflection of the sphenoid ridges of the lateral wall of the skull on each side	6/8/35 Definite diminution in size of lesions	10/11/35 Lesions practically clear					
Ribs	3/28/35 Irregularity of outline and consistency in the proximal part of the 1st left rib, at the vertebral ends of the 4th, 5th and 6th ribs in the left and midpart of the 9th rib, posterior left	6/8/35 Moderate repair of all lesions	10/11/35 No change	4/10/36 Lesions in all ribs completely healed	8/19/36 Normal	12/7/36 Normal	3/25/37 Normal	6/5/37 Normal
Iliac bones	4/10/35 Lytic lesions in midportion of the left iliac bone; similar lesion with sclerotic border in the upper part of the left iliac bone	6/8/35 Moderate repair of all lesions	10/11/35 Complete healing of all lesions					
Lower extremities	3/28/35 Rarefied circumscribed lesion in the proximal diaphysial end of each tibia and in the proximal diaphysial end of the left fibula	6/8/35 Regression of all lesions	12/9/36 Complete clearing of all lesions					

child was discharged in three weeks and did not return to the hospital again until December 2. At this visit, on clinical and roentgen examination the spinal fusion was found to be solid and the paravertebral abscess involuting. There was ankylosis of the right shoulder, probably fibrous, but the patient made no complaint. A roentgenogram of the chest showed no pathologic condition, and there

Fig. 4.—Roentgenogram taken two and one-half months after the patient's admission, showing moderate repair of all lesions in the left humerus.

was no evidence of activity or of change in the lesions of the other bones except in those of the right humerus.

After another three month period of care at home with use of the frame, the patient returned to the hospital on March 12, 1937, complaining of pain in the right shoulder, although otherwise she was asymptomatic and in good general

condition. There were pain and marked limitation of motion in the right shoulder. The spinal fusion appeared solid clinically and on roentgen examination. Roentgen examination of the right shoulder revealed an increase in the destruction involving the head of the humerus. However, the general condition of the child appeared excellent, in spite of the increased destruction at this site. The sedimentation rate was 0.61. The patient was allowed to be up for short periods during the day wearing a Taylor back brace. This resulted in daily elevation in temperature to 101.5 F.

On June 26 the child was transferred to a tuberculosis sanatorium for further care in order to be removed from contact with the infections met in a general children's ward.

Fig. 5.—Roentgenogram of the left humerus, showing complete healing of all lesions seventeen months after the patient's first admission.

DIFFERENTIAL DIAGNOSIS

Multiple cystic osseous lesions in childhood are rare, and their accurate interpretation depends on a consideration of several diseases which may produce them.

The more common diseases which may produce chronic multiple cystic osseous lesions are tuberculosis, syphilis and osteomyelitis. Hyperparathyroidism, the xanthomas and multiple myeloma are infrequently seen, but they call for careful differentiation. Frequently the symptoms and clinical picture must be augmented by careful ancillary examination,

including roentgenograms, chemical analysis of the blood, serologic tests, biopsy and bacterial culture.

In cases in which tuberculous cystic osseous disease is suspected, a history of contact with tuberculosis or of the ingestion of raw milk, symptoms of tuberculous infection and a positive tuberculin test are positive indications. Roentgen evidence of childhood pulmonary tuberculosis is strongly suggestive of the cause of the osseous lesions. In the majority of recorded cases, the primary lesion was intrathoracic. The roentgenogram shows diaphysial tuberculous lesions to be circumscribed areas of rarefaction with little sclerosing reaction. Periosteal proliferation or cortical expansion may be absent, and formation of an abscess or sequestration is seldom encountered.

Syphilis of the shafts of long bones may produce tenderness, nocturnal pain or deformity. In some cases the paucity of physical signs makes differentiation dependent on the Kahn test or on the roentgenologic appearance. Syphilis is primarily a periosteal reaction affecting the tibia, the ulna, the radius and the cranium in the order named.

Chronic pyogenic osteomyelitis produces multiple circumscribed areas of bone destruction, usually involving the metaphysis. It may progress to sequestration and to sinus formation. The roentgenogram is characterized by localized sclerosis and by adjacent subperiosteal bone formation. Biopsy or laboratory aids may be necessary for diagnosis.

Hyperparathyroidism, or von Recklinghausen's disease of the bones, is rare in the young. Conspicuous symptoms are pain and tenderness in the bones accompanied with loss of weight and of muscular tone. Multiple cystic areas are caused by abnormal calcium metabolism dependent on parathyroid adenoma. Considerable diagnostic importance may be placed on an increased excretion of calcium and on a lowering of the phosphorus of the blood serum, with an elevation of the calcium of the serum when skeletal changes are present. The course of the disease is protracted and the prognosis favorable. The roentgenogram shows general rarefaction and diffuse lytic changes with cystic formations developing in the pelvis, in the spine and in the metaphyses of the long bones. Rarely are the ribs or the skull involved.

The xanthomas, which are characterized by disturbances in lipoid metabolism and which produce changes in the bones, lymph nodes, spleen, liver and reticuloendothelial system, include Schüller-Christian, Gaucher and Niemann-Pick disease.

Though uncommon at any age, Schüller-Christian disease usually appears during childhood. Clinical manifestations are exophthalmos, pigmentation of the skin, diabetes insipidus and splenomegaly. Defects in the bones of the skull are prominent clinically and in roentgenograms. The bones affected are the skull, the pelvis and the scapula, with the ribs

occasionally and the long bones rarely. The roentgenograms show irregular annular rarefaction without peripheral reactions. There may be areas of involvement and areas of regression.

Gaucher's disease usually occurs in patients between the ages of 3 and 10 years. Symptoms are great enlargement of the spleen, rheumatic pains in the long bones, pigmentation of the skin, anemia and leukopenia. The long bones are usually affected, especially the femur and the pelvis. Small areas of bone destruction without periosteal reaction may be present, but the outstanding characteristic is a change in the contour of the femur, likening it to an Erlenmeyer flask. In Niemann-Pick disease the bones are seldom involved.

Multiple myeloma is exceedingly rare in childhood. The onset may be with vague rheumatic pains, weakness and lassitude. Later there are tumors, loss of strength in the legs and pronounced anemia. Rapid progression with fatal termination in two years is the usual course. The sternum, ribs, spine, pelvis and upper end of the femur are characteristically involved. The roentgenogram demonstrates multiple central punched-out areas a centimeter in diameter, or occasionally a diffuse rarefied osteoporotic appearance is seen.

At times coccidioidal granuloma, enchondroma, leprosy and a metastatic malignant process must be considered in the differential diagnosis.

CONCLUSIONS

Analysis of the cases of osteitis tuberculosa multiplex cystica reported by Jüngling and of similar cases reported since 1928 in adults [5] and in children shows:

1. The disease may occur in children as well as in adults.

2. The presence of cutaneous lesions is not necessary for diagnosis. Such lesions are usually not present in children, or they may appear only after the disease has been present for several years.

3. The pathologic process is an entity with varying degrees of involvement and destruction of bone. The difference in the degrees of osseous involvement does not necessitate nomenclature other than mention of the anatomic location or than such a designation as disseminated cystic tuberculosis of the bones.

4. The cystic changes in bone may involve only the small bones of the hands and feet, only the long hollow bones or both. Classification with restriction to Jüngling's description, in which only the hands or

5. Sanes, S., and Smith, W. S.: Osteitis Tuberculosa Multiplex Cystica of the Fibula and Tibia, J. A. M. A. **102**:1206 (April 14) 1934. Van Alstyne, G. S., and Gowen, S. H.: J. Bone & Joint Surg. **15**:193, 1933. Petter and Medelman.[4b]

the feet are affected, or, with restriction to Kienböck's description,[6] in which only the long hollow bones are involved, is not necessary, as the disease process has the same cause in both instances.

5. The primary focus of tuberculous infection in nearly all cases is probably intrathoracic. In view of the negative results of both the tuberculin test and the guinea pig inoculation and in view of the absence of tubercle bacilli in the stained sections, the strongest supporting evidence for tuberculous causation of the bone lesions in Jüngling's cases was the thoracic involvement. Subsequently it has been demonstrated by Stalmann [3e] and others [4b] that tubercle bacilli may be recovered from the lesions of bone, thus conclusively showing the tuberculous origin of the disease.

6. The roentgenologic appearance of the osseous lesions is reasonably characteristic and is of distinct diagnostic value.

The paucity of reports in the literature depends largely on the absence of localizing signs, especially in cases in which the long hollow bones are involved, and on failure to take a roentgenogram of the part.

SUMMARY

The characteristics of the disease osteitis tuberculosa multiplex cystica, as described by Jüngling in adolescents and in adults, is summarized. It is pointed out that the disease occurs also in children. The classification of the disease into types is dispensed with, as each type is merely a different degree of a pathologic process and reference to the anatomic location of the lesion is sufficient.

The history, physical findings, results of laboratory studies, picture shown by serial roentgenograms and progress of the disease in a girl of 6 years, in whom the long bones were affected, are reported. The small bones of the hands and feet were involved.

In a collection of cases of osteitis tuberculosa multiplex cystica in children since 1929, it is seen that the disease process attacked the diaphyses of the long bones and the small long bones of the hands and feet, in combination or separately, with equal frequency. The onset of the disease in children is described as gradual and, in contrast to the onset in adults, as accompanied with few or no localizing symptoms or signs. Toxemia and fever are usually absent. In the 10 cases collected there were few symptoms referable to the lesions. The cystic lesions of the bone are frequently detected accidentally at the time of taking roentgenograms of other parts.

Two thirds of the patients, including ours, gave roentgenologic evidence of primary pulmonary tuberculosis, probably indicating that the

6. Kienböck, R.: Arch. f. orthop. u. Unfall-Chir. **29**:67, 1931.

original focus was in the pulmonary region. The cystic lesions in all cases but 1 tended to heal slowly. There was complete bony repair in 2. Treatment consisted of general treatment for tuberculosis or care in a sanatorium, with additional individual symptomatic measures (operation has been beneficial to some adults).[4b]

It is maintained that differential diagnosis of cystic osseous lesions of doubtful causation should include tuberculosis, syphilis, osteomyelitis, xanthomas, hyperparathyroidism, multiple myeloma, coccidioidal granuloma, leprosy and enchondroma.

PARATYPHOID FEVER COMPLICATED BY MULTIPLE FOCI OF OSTEOMYELITIS

REPORT OF A CASE WITH POSTMORTEM OBSERVATIONS

WALTER W. JETTER, M.D.
BUFFALO

Paratyphoid fever due to infection with Salmonella schottmülleri (Bacillus paratyphosus B) is not uncommon. Zinsser and Baynes-Jones [1] stated that its incidence may assume epidemic proportions, as occurred during the World War. While the condition may be severe and typhoid-like, the mortality seems to be low: 1.5 per cent, according to Cecil,[2] as compared to the 10 per cent mortality of typhoid fever. The incidence of severe complications is correspondingly small. Whereas suppurative lesions of the bones occur frequently in cases of typhoid fever, Veal and McFetridge in 1934 [3] were able to collect but 18 cases of similar complications from the extensive literature on paratyphoid fever. The following case is presented not only because of the unusual, widespread involvement of the bone but because of the severity of the visceral manifestations.

REPORT OF A CASE

History.—For five weeks prior to her admission to the Buffalo City Hospital the patient, a white girl aged 10 years, was constipated and had hard, dry stools. Once or twice a week there would be a watery stool described as grayish green and of the consistency of pea soup. The appetite was poor. Later, anorexia and occasional night sweats developed, and it was noticed that the skin was becoming progressively more pale. Thirteen days before admission the girl suffered a severe beating pain just below the knee. Swelling, heat and redness developed, but these did not incapacitate the child at first. However, the pain and swelling became worse, medical attention was sought, and hospitalization was advised.

Physical Examination.—On admission to the hospital, the girl's skin appeared pale and she was emaciated. The temperature was 100 F.; the pulse rate was 90 and the respiratory rate 25 per minute. The chest was clear. The heart sounds

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From the Department of Pathology, Buffalo City Hospital and the University of Buffalo.

1. Zinsser, H., and Bayne-Jones, S.: Textbook of Bacteriology, ed. 7, New York, D. Appleton-Century Company, Inc., 1935, p. 568.

2. Cecil, R. L.: Textbook of Medicine, ed. 3, Philadelphia, W. B. Saunders Company, 1936, p. 167.

3. Veal, J. R., and McFetridge, E. M.: Paratyphoid Osteomyelitis: Report of Two Additional Cases, J. Bone & Joint Surg. **16**:445, 1934.

were of poor quality. The abdomen was soft and flabby, but the spleen and liver were not palpable. A circumscribed, tender, slightly swollen area of the size of a half-dollar was found over the left tibia, about 2 inches (5 cm.) distal to the knee joint. The clinical impression was acute osteomyelitis. Roentgen examination confirmed the diagnosis, revealing an area of rarefaction in the upper third of the shaft of the left tibia, 2 inches (5 cm.) from the knee joint.

Laboratory Examinations.—Examination of the blood showed 2,400,000 red cells per cubic millimeter, a 40 per cent hemoglobin content by the Sahli method and 7,900 white cells. Differential study revealed 40 per cent unsegmented and 13 per cent segmented neutrophils, 45 per cent lymphocytes and 2 per cent monocytes. Chemical examination of the urine and blood gave no remarkable findings, and the Wassermann reaction was negative.

Course.—Operation on the day following the patient's admission disclosed thickening and inflammation of the periosteum over the left tibia at a point 2 inches below the knee. There was a small collection of subperiosteal pus. Drill holes were made in the tibia, and pus was obtained. On a direct smear no organisms were seen, but cultures of the material revealed a gram-negative bacillus in pure culture. This had the characteristic fermentative and agglutinative reactions of B. paratyphosus B, agglutinating with known paratyphoid B serum up to a dilution of 1 : 300,000. A culture of blood taken on the same day yielded the same organism. The blood serum had an agglutination titer of 1 : 1,280 for the B strain but only 1 : 20 for the A and for Bacillus typhosus.

The immediate postoperative course was fairly good. Drainage from the operative lesion was moderate. While the temperature dropped at times to almost normal levels, the blood culture remained positive throughout the illness. On the thirteenth day following admission an infection of the upper respiratory tract developed, the temperature rising to 103 F. On the fifteenth day the liver was palpable. Purpuric spots appeared on the left forearm (Rumpel-Leede phenomenon). The condition of the respiratory tract was unchanged. The stools were not abnormal. On the twenty-first day pain had developed in the left ear. The tympanic membrane was bulging. On incision, pus was obtained, the smears showing streptococci. The abdomen was moderately distended and tympanitic, and both the liver and the spleen were now palpable. A transfusion of 200 cc. of whole blood was administered.

On the twenty-fifth day the temperature had risen to 105 F. The child now complained of tenderness of both legs and of the left forearm. Roentgen examination of the skeletal system exhibited multiple osteomyelitic processes in the upper third of the shaft of both the right and the left tibia and fibula; scattered lesions in both humeri, in the right pubis and ischium and in the right ulna and radius, and suspicious areas in both femurs. A second transfusion of blood (250 cc.) was given. No surgical procedure was contemplated because of the multiplicity and extent of the lesions, the inaccessibility of some and the poor condition of the patient. A blood count showed 7,200 white cells, with 29 per cent unsegmented and 9 per cent segmented neutrophils, 60 per cent lymphocytes and 2 per cent monocytes.

The patient was becoming steadily worse. Many purpuric spots made their appearance on the trunk and extremities. The agglutination titers of the blood serum were 1 : 1,280 and 1 : 640. Study of the blood on the thirty-sixth day revealed 10,900 white cells with 45 per cent unsegmented and 5 per cent segmented neutrophils, 48 per cent lymphocytes and 2 per cent monocytes. Death occurred thirty-nine days after the child's admission.

Fig. 1.—*A*, roentgenogram showing destruction of bone in the upper third of the right tibia and fibula, with marked periosteal reaction, more marked in the tibia. *B*, destructive osteomyelitic process involving the proximal two thirds of the shafts of the right radius and ulna. There is considerable periosteal reaction in the middle third of the radius.

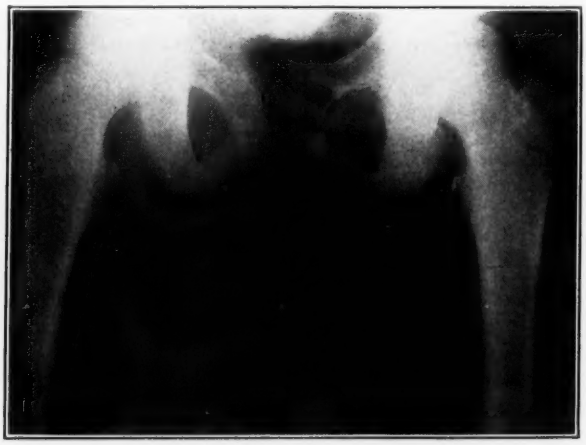

Fig. 2.—Roentgenogram showing marked destruction of the right os pubis and the horizontal ramus of the os ischii.

Postmortem Examination.—Gross Observations: There were extreme pallor and emaciation. The skin of the abdomen, chest and extremities showed many discrete circular reddish brown petechiae varying in diameter from pinpoint to 0.5 cm. The brain was wet and edematous. Pus containing streptococci was found in both middle ears and in the left frontal sinus. The pericardium and pleura exhibited many discrete petechiae. The pericardial sac contained 350 cc of clear straw-colored fluid. The heart was dilated, particularly the right auricle and ventricle, and the musculature was flabby and pale. The lungs showed only congestion and edema. Hyperplasia and occasional ovoid shallow ulceration occurred in Peyer's patches in the terminal portion of the ileum. The mesenteric nodes were swollen, the size varying from that of a pea to that of a bean, and their soft and fleshlike consistency was apparent on section. The liver weighed 2,220 Gm. The cut surface was dull brown and opaque, and over it numerous yellowish flecks, 3 mm. in diameter, were dispersed. The spleen weighed 450 Gm.; it was soft and deep red. Section revealed soft, overflowing pulp; the malpighian bodies were obscured. Discrete and punctate petechiae were encountered on both the surfaces of the kidneys. The cut surfaces showed ovoid areas of a color alternating between brilliant red and yellow and with a diameter varying from 1 to 3 cm. The lesions almost completely obliterated the few remaining areas of normal kidney parenchyma, which were salmon red. The skeletal system showed multiple discrete ovoid grayish red areas of softening in the right pubis, ischium, radius and ulna and in both femurs, humeri, tibias and fibulas. No large sequestrums were noted. The cortex adjacent to these areas was destroyed in part, and the periosteum was greatly thickened and fragmented. The exudate showed many mononuclear and some polymorphonuclear leukocytes. B. paratyphosus B was recovered subsequently.

Microscopic Observations: The spleen contained small areas of necrosis in Billroth's cords and large accumulations of mononuclear cells in the red pulp. The lymphoid nodules and the medullary cords of the lymph nodes were obliterated in part, owing to a similar infiltration of mononuclear cells which packed the sinuses. There were many small patchy areas of focal necrosis in the liver. The kidneys exhibited large dense collections of cells of the mononuclear type, with considerable hemorrhagic infiltration, the lesions corresponding to the red and yellow areas noted grossly. In these areas there was marked necrosis of the kidney parenchyma. Sections of the lesions of the bone showed inflammatory granulation tissue in the medullary and haversian canals. The predominating type of cell was mononuclear. Scattered here and there were large foci of hemorrhage, while in other areas there were smaller patches of granular débris in which some necrotic polymorphonuclear leukocytes were seen. The trabeculae were thinned and somewhat rarefied, and the cortex was narrowed. The periosteum was thickened, edematous and infiltrated with many mononuclear cells.

COMMENT

Osteomyelitis complicating typhoid fever is not particularly uncommon: Winslow [4] estimated that in 0.82 per cent of all cases of typhoid fever this finding is exhibited. Osteomyelitis of paratyphoid origin is

4. Winslow, N.: Typhoidal Osteomyelitis, Ann. Surg. **77**:319, 1923.

more rare, however, even when one takes into consideration the comparative infrequency of paratyphoid fever. The rarity of osseous complications is explainable in cases in which the paratyphoid infection produces the so-called food poisoning syndrome, which is characterized by acute onset, fever, prostration, rapid pulse, nausea and vomiting, with subsidence of symptoms in a few days. When the picture suggests typhoid fever, however, as is frequently the case, especially with the paratyphoid B strain, one would expect the complication of osteomyelitis as often as with true typhoid fever. There are the same localization and proliferation of the organism in Peyer's patches and the same bacterial dissemination in the blood stream, with invasion of the skeletal system possible at any time.

According to Veal and McFetridge,[3] who have surveyed the literature, the condition occurs in the late stages of paratyphoid fever or during convalescence. The onset is acute or subacute, but the acute clinical manifestations so often found with pyogenic infection are not present. In our present case, the complication of osteomyelitis occurred in the fourth week of the disease. Its onset was subacute, the patient suffering little disability for at least ten days. Usually the lesions are single, involving, as a rule, the tibias, ribs or sternum. My report is of interest because of the widespread dissemination of the lesions. Only 1 other case has been described in which there was multiple involvement, that of Carrington and Davison in 1925.[5]

There are no findings specific of invasion by the paratyphoid bacillus. As in the present case, however, preceding malaise, lassitude and mild fever, plus absence of marked tenderness at the site of the lesion, with little resulting disability, should arouse suspicion of typhoid-paratyphoid infection. The leukocyte count may be normal or lowered, but in some of the recorded cases leukocytosis was shown. In the present case, at the time of the patient's admission there were 7,900 white blood cells per cubic millimeter with neutropenia and a shift, a finding consistent with the diagnosis of a bacillary infection. Although absolute diagnosis can be made only by identification of the organism in material obtained from the osseous lesion, the finding of the paratyphoid organism on blood culture is strong presumptive evidence that the osteomyelitic process is caused by the same bacteria. A high agglutination titer is of almost equal significance. In this case B. paratyphosus B was isolated in the material from the original focus in the left tibia. The blood culture was positive on all three occasions over a period of five weeks, which pointed to continuous bacteremia during that time. That a high

5. Carrington, G. L., and Davison, W. C.: Multiple Osteomyelitis Due to Bacillus Paratyphosus B, Bull. Johns Hopkins Hosp. **36**:428, 1925.

agglutination titer does not necessarily offer a good prognosis is evidenced by the fatal outcome in the present case, in which there were the extremely high titers of 1:1,280 and 1:640.

SUMMARY

A case of paratyphoid fever due to S. schottmülleri and ending fatally is described, with the postmortem observations. A remarkable number of foci of osteomyelitis were present. As far as can be determined, it is the nineteenth recorded case of osteomyelitis complicating paratyphoid fever and the second in which the foci were multiple.

Progress in Pediatrics

BRONCHIECTASIS IN CHILDREN

WITH SPECIAL REFERENCE TO PREVENTION AND EARLY DIAGNOSIS

ANTOINETTE RAIA, M.D.
NEW YORK

The fact that the patient with bronchiectasis is a chronic invalid, whose life expectancy is shortened by ever recurring attacks of pneumonia, makes the condition one of the most dreaded of pulmonary afflictions. With the general acceptance of the conviction that bronchiectasis in adults frequently has its inception in early life, the importance of the disease in children is receiving increasing attention. As with preventive measures in all branches of medicine, the interest in this particular condition has been extending more and more to early recognition and especially to prevention.

This study has been undertaken with the object of finding the essential causes which contribute to the formation of bronchiectasis and of discovering the earliest clinical picture which requires watching.

Material for this study has been provided by the chest clinic of the children's medical service of Bellevue Hospital. The detailed analysis of the history, symptoms, physical signs and roentgenograms by which the fundamental factors leading to the diagnosis of bronchiectasis are pointed out has also been applied in a series of other cases in which chronic or recurrent symptoms of the respiratory tract have occurred in varying degrees. From the data thus obtained three distinct groups have emerged: the group with well established bronchiectasis, the group with early or minimal bronchiectasis and the group with a prebronchiectatic condition or with potential bronchiectasis. It is in the second and third of these groups that much preventitve work can be done, for by the institution of proper therapeutic measures it will be shown that the progression of minor lesions into more serious ones may be arrested.

THE GROUP WITH WELL ESTABLISHED BRONCHIECTASIS

The cases of 33 of a number of patients with bronchiectasis admitted to the Children's Medical Service of Bellevue Hospital in the last six years have been selected for analysis. Similar clinical

From the Department of Pediatrics, New York University, and the Chest Clinic of the Children's Medical Service of Bellevue Hospital.

surveys on children have been conducted, especially in recent years, by numerous observers, notably by Armand-Delille,[1] Thorpe,[2] Findlay and Graham,[3] Nobécourt,[4] Lemon[5] and Boyd.[6] The study of these (table 1) is presented in some detail because it supplies the data on which the recognition of the early and potential stages of bronchiectasis is based.

DIAGNOSTIC CRITERIA

History.—Pneumonia: The story of illness dated from an attack of pneumonia in two thirds of the cases (67 per cent). This etiologic pneumonia occurred in the first six years of life in 13 children, of whom 6 were infants. In only 6 was this pneumonia apparently uncomplicated, and of these, 4 had the disease in infancy, 1 at the age of 5 years and 1 at the age of 6 years. As for the other children, the pneumonia followed measles in 4 and pertussis in 2 and was complicated by empyema with operation in 5. In 2 patients pneumonia occurred in the presence of enlarged tuberculous nodes, and in another, bronchiectasis was secondary to a postpneumonic abscess. Empyema occurred in 5 children between 6 and 8 years of age.

Bronchitis: A history of bronchitis was given by 11 patients, or one third. In only 1, however, was the illness dated from an attack of bronchitis occurring in infancy. It seems reasonable to assume that in this case the initial bronchitis was probably bronchopneumonia, when it is remembered that the two diseases are sometimes differentiated with difficulty. In the other cases the attacks of bronchitis were instances of the repeated intercurrent infections to which the children with this condition are subject.

Pertussis: This disease had occurred in 15 cases. In 7 of these children, all 6 years of age or under, the symptoms were dated from an attack of this illness; 2 of the 7 had complicating pneumonia.

Measles: Twenty-nine children gave a history of measles; 4 of these had been ill since contracting this disease. However, in all 4 cases

1. Armand-Delille, P. F.; Lévy, R., and Marie, J.: Les formes cliniques de la dilatation des bronches chez l'enfant et leur diagnostic lipiodo-radiologique, Rev. franç. de pediat. **1**:125 (Aug.) 1925.

2. Thorpe, E. S., Jr.: Chronic Bronchiectasis in Childhood with Observations on Early Diagnosis, Am. J. M. Sc. **177**:759 (June) 1929.

3. Findlay, L., and Graham, S.: Bronchiectasis in Childhood: Its Symptomatology, Course and Cause, Arch. Dis. Childhood **2**:71 (April) 1927; Prognosis in Bronchiectasis, ibid. **6**:1 (Feb.) 1931.

4. Nobécourt, P.: Les dilatations des bronches dans le grande enfance, Rev. gén. de clin. et de thérap. **43**:833 (Dec. 21) 1929.

5. Lemon, W. S.: Bronchiectasis in Childhood, M. Clin. North America **10**:531 (Nov.) 1926.

6. Boyd, G. L.: Bronchiectasis in Children, Canad. M. A. J. **25**:174 (Aug.) 1931.

measles was complicated by pneumonia and in 1 of them it was followed by pertussis and pneumonia in close succession. In these cases measles occurred at the ages of 4, 5, 6 and 8 years, respectively. Therefore measles unless complicated by pneumonia was not a responsible factor in any instance, whereas pertussis without a history of pneumonia was noted as the cause of subsequent symptoms in 6 cases. Here again the possibility exists, especially when it is realized that these children come from poor districts, where the physician is not called unless a child is obviously ill, that pulmonary findings and evidences of low grade infection were probably present in many if not all of the cases of pertussis which left sequelae.

Pneumonia, then, and those diseases which predispose to pneumonia, namely measles and pertussis, accounted for the bronchiectasis in 24 (73 per cent) of the 33 cases. The causes in the remaining 9 cases were as follows:

Pressure by Tuberculous Lymph Nodes: This resulted in bronchial stenosis in 2 cases, with consequent collapse of the middle lobe of the right lung in case 21, and of both the upper and the lower lobe of the left lung in case 7 (table 1). To this element of deficient pulmonary ventilation was added infection in the form of acute pneumococcic pneumonia. In the presence of the combined factors of infection and prolonged obstruction of drainage, bronchiectasis was the inevitable result. Indeed, the pathogenesis of bronchiectasis was demonstrated clinically in these cases under circumstances that may be said to have closely simulated controlled experimental conditions.

Post-Tonsillectomy Abscess: In 3 children bronchiectasis was secondary to post-tonsillectomy abscess (cases 8, 9 and 30).

Foreign Body: In the 4 remaining cases the cause was a foreign body. Again the combined factors of infection with resultant fibrosis and obstruction of drainage came into play. One of these children (case 23), in whom the foreign body (a nail) was removed one year after inhalation, is free from symptoms at the time of writing. Seven years after the accident he came under observation for a minor illness. The only clue to his diagnosis was offered by the roentgenogram, which showed perfectly clear pulmonary fields but a slight retraction of the mediastinum to the right. Injection of iodized poppyseed oil revealed saccular bronchiectasis of minimal extent in the lower lobe of the right lung. The presence of the nail in the lung for one year brought about fibrosis, as evidenced by the retraction of the mediastinum, and localized bronchiectasis. A clinical cure, which at the time of writing has lasted for twelve years, followed removal of the nail, even though there has been no anatomic recovery. In the other 3 cases, the foreign body was not removed, and the involved lung was the site of advanced suppuration. In 2 of these the diagnosis was confirmed by the broncho-

gram. One child (case 20) died after lobectomy for cylindric bronchiectasis of the lower lobe of the right lung. The other (case 12), with extensive bronchiectasis of the entire left lung and a large abscess of the upper lobe of this lung, was clinically cured after drainage by thoracotomy. The third child (case 31), who was too ill for a bronchogram and in whose case there was no doubt as to the suppurative nature of the lesion, died of an abscess of the brain.

Briefly, there is no case of bronchiectasis in this group in which preceding infection was not known to have been present. Obstruction was not always so readily demonstrated, but it was shown to have existed in a sufficient number of cases to justify the assumption of its presence in similar cases. Perhaps the best evidence of the important role played by inadequate drainage is given by the 6 cases in this series (7, 14, 21, 26, 28, 30) in which the patient came under observation during the initial illness which resulted in bronchiectasis. They will be referred to later in this study; suffice it to say at this point that infection and mechanical obstruction to drainage were present in all 6.

Symptoms.—The outstanding symptoms were cough and expectoration.

Cough: This occurred in all cases except that of a boy of 8 years whose only symptom was hemoptysis. The character of the cough is noteworthy. It was loose, deep and not violent, but it made one feel that the patient *ought* to expectorate. Its frequency varied with the amount of expectoration and with changes in posture. In 85 per cent of those with cough it was a constant symptom, with varying severity but with no free intervals. In the remaining 15 per cent the cough cleared after it had existed for years.

Expectoration: This was a symptom in 91 per cent of the cases studied. The actual percentage is probably even higher, for those children who had no complaint of expectoration belonged to the young age group, in which it is usually swallowed. Expectoration was a constant symptom in all but 6 cases. In these it had existed over a long period in the past but either had cleared completely during the follow-up period or had cleared only to recur periodically during acute exacerbations. The sputum was foul smelling in about half the cases and whether scant or profuse was typically nummular and purulent.

Other Symptoms: Manifestations of less frequent occurrence were hemoptysis, in 6 cases; pain in the chest, in 5 cases; dyspnea, in 4 cases, and cyanosis, in 4 cases.

Physical Signs.—Signs of chronic consolidation, consisting mainly of impaired resonance and bronchial breathing, were present in 20 cases. In addition, cavernous or tubular breath sounds were found at one time or another in 13 of these cases. Not infrequently the physical findings

TABLE 1.—*Résumé of Thirty-Three Cases of Bronchiectasis*

Case	Age of Initial Illness	Etiology	Anatomic Diagnosis‡ (Made by Bronchogram)	Functional Diagnosis	Treatment	Present Status
1	8 yr.	Pneumonia; empyema (thoracotomy)	Saccular L.L.L.	Severe	Lobectomy	Improved
2	6 yr.	Pneumonia; empyema (thoracotomy)	Seccular R.M.L.	Severe	Postural drainage	Clinically cured
3	7 yr.	Pneumonia; empyema (thoracotomy)	Saccular L.L.L.	Severe	Postural drainage	Died of pneumonia at 10 yr.
4	8 yr.	Pneumonia; empyema (thoracotomy)	Saccular L.L.L.	Severe	Lobectomy	Clinically cured
5	9 yr.	Pneumonia → abscess	Saccular R.L.L.	Severe	Postural and bronchoscopic drainage	Died of osteomyelitis of femur at 11 yr.
6	2 yr.	Pertussis	Saccular R.M.L.	Severe	Postural and bronchoscopic drainage	Unimproved
7*	3 yr.	Bronchostenosis by tuberculous nodes; bronchopneumonia	Saccular L.L.L.	Severe	Postural and bronchoscopic drainage	Unimproved
8	3 yr.	Post-tonsillectomy abscess	Saccular R.U.L., R.M.L., R.L.L.	Severe	Lobectomy	Clinically cured
9	7 yr.	Post-tonsillectomy abscess	Saccular R.U.L.	Moderate	Thoracotomy for ruptured abscess	Clinically cured
10	1 mo.	Pertussis	Saccular R.U.L., L.U.L.	Moderate	Postural drainage; treatment of sinuses	Improved
11	8 yr.	Measles-pneumonia	Saccular R.M.L.	Moderate	None	Improved
12	4 yr.	Abscess secondary to foreign body (?)	Saccular-cylindric L.U.L., L.L.L.; abscess L.U.L.	Severe	Thoracotomy	Clinically cured
13	4 yr.	Pertussis	Saccular R.L.L.; cylindric L.L.L.	Severe	Postural drainage; treatment of sinuses; autogenous vaccine	Unimproved
14*	4 yr.	Three attacks of pneumonia; pertussis	Saccular-cylindric L.U.L., L.L.L.	Severe	Postural drainage; occasional bronchoscopic treatment	Unimproved
15	6 yr.	Measles-pneumonia	Saccular-cylindric L.L.L.	Moderate	Postural and bronchoscopic drainage	Improved
16	2½ yr.	Pneumonia	Saccular R.L.L.; cylindric L.L.L.	Moderate	Postural drainage; autogenous vaccine; diathermy	Unimproved
17	Infancy	Bronchitis	Cylindric L.L.L.	Moderate	Postural drainage; treatment of sinuses	Unimproved

16	2½ yr.	Pneumonia	Saccular R.L.L.; cylindric L.L.L.	Moderate	Postural drainage; autogenous vaccine; diathermy	Unimproved
17	Infancy	Bronchitis	Cylindric L.L.L.	Moderate	Postural drainage; treatment of sinuses	Unimproved
18	4 yr.	Measles-pneumonia	Cylindric L.L.L.	Moderate	Postural drainage; treatment of sinuses; tonsillectomy	Unimproved
19	6 yr.	Pertussis	Cylindric L.L.L.	Moderate	Postural drainage; treatment of sinuses; occasional bronchoscopic treatment	Improved
20	11 yr.	Foreign body (peanut)	Cylindric R.L.L.	Moderate	Lobectomy	Died of brain abscess after lobectomy
21*	15 mo.	Bronchostenosis by tuberculous nodes; bronchopneumonia	Cylindric R.M.L.	Moderate	Care in sanatorium	Improved
22	1 mo.	Bronchopneumonia	Minimal saccular R.L.L.	Moderate	Postural drainage	Unimproved
23	2 yr.	Foreign body (nail)	Minimal saccular R.L.L.	Dry	Bronchoscopic removal of nail	Clinically cured
24	8 yr.	Pneumonia; empyema (thoracotomy)	Minimal saccular L.L.L.	Dry (hemoptysis)	None	Clinically cured
25	6 yr.	Pneumonia	Minimal cylindric L.L.L.	Moderate	Postural drainage; treatment of sinuses	Improved
26*	5 yr.	Measles-bronchopneumonia	Minimal cylindric R.L.L.	Dry	Postural and bronchoscopic drainage; treatment of sinuses; tonsillectomy	Cured; second bronchogram normal
27	5 yr.	Measles-pertussis-pneumonia	Minimal cylindric L.L.L.	Moderate	Postural and bronchoscopic drainage; treatment of sinuses; tonsillectomy	Improved; second bronchogram unchanged
28*	6 yr.	Pneumonia	Minimal cylindric R.L.L.	Dry	Postural and bronchoscopic drainage; treatment of sinuses	Cured; second bronchogram normal
29	1 yr.	Pneumonia	Minimal cylindric L.L.L.	Moderate	Postural drainage	Improved
30*	5 yr.	Post-tonsillectomy abscess	Minimal cylindric R.L.L.	Moderate	Postural and bronchoscopic drainage	Improved
31†	2 yr.	Foreign body (chicken bone)	Suppuration R.L.L.	Severe	Postural drainage	Died of brain abscess at 7 yr.
32†	5 yr.	Pneumonia	Bilateral pneumonia; suppuration	Severe	Admitted in terminal stage	Died of pneumonia at 10 yr.
33†	18 mo.	Pertussis-pneumonia	Suppuration right lung	Severe	Postural drainage	Died of pneumonia at 2½ yr.

* Observed during initial illness.

† Too ill for bronchogram.

‡ In this and in the other tables R.U.L. indicates upper lobe of right lung; R.M.L., middle lobe of right lung; R.L.L., lower lobe of right lung; L.U.L., upper lobe of left lung, and L.L.L., lower lobe of left lung.

suggested the presence of one large cavity, yet the bronchogram gave evidence of numerous bronchiectatic cavities. Of these 20 cases, in only 2 has consolidation been observed to clear, in 1 after many months and in the other after ten years. In 7 cases there were signs of pneumonia that resolved very slowly; in only 3 of these did the signs disappear entirely. In the remaining 4, consonating or moist rales remained constantly at the site of the lesion. This makes a total of 27 cases, or 82 per cent, in which signs of prolonged consolidation were the characteristic pulmonary findings. In 9 cases the findings consisted chiefly of rales, either persistent or frequently recurring over the same area. In summary, signs chronically present over one area or slowly clearing signs with a tendency to recur at the same site form a striking feature of bronchiectasis. In some cases few or no signs occur, especially when involvement is of the dry type, but these cases are in the minority.

Clubbing of the fingers was found in 13 children; it was most marked in those with extensive pulmonary lesions.

Roentgen Findings.—Chest: Pnuemonic shadows of varying descriptions were present in two thirds of the cases (22). In 9 of these the shadow was persistent and localized, found most often in the lower lobes and tending to obliterate the cardiodiaphragmatic angle, while in 3 it revealed persistent disseminated nodular infiltration. In 7 cases the pulmonary consolidation was combined with evidences of cavitation. Slow clearing of the shadow occurred in 6 cases.

Evidence of pleural involvement, either as axillary or interlobar thickenings or as a uniform density extensive enough to obscure the underlying intrapulmonary disease, was found in 11 cases.

Evidence of fibrosis was also frequent. In 9 cases it was so extensive as to result in displacement of the mediastinum, while in 5 cases its presence was indicated by an increase in the bronchial markings, usually at the base. Two children presented the triangular shadow characteristic of a shrunken, fibrotic lobe.[7]

In 3 cases occurred transient collapse of a lobe with subsequent complete reexpansion.[8]

The honeycomb appearance sometimes described as pathognomonic of bronchiectasis was infrequent in our experience.

It can be said, therefore, that the outstanding roentgen findings were those of persistent pulmonary infiltration and fibrosis. The diagnostic significance of such infiltration is emphasized when it is observed that the introduction of iodized poppyseed oil in such areas has never failed

7. Jones, O. R., and Cournand, A.: The Shrunken Pulmonary Lobe with Chronic Bronchiectasis, Am. Rev. Tuberc. **28**:293 (Sept.) 1933.

8. Anspach, W. E.: Atelectasis and Bronchiectasis in Children: A Study of Fifty Cases Presenting a Triangular Shadow at the Base of the Lung, Am. J. Dis. Child. **47**:1011 (May) 1934.

to reveal the presence of bronchiectasis. It is also noteworthy that, as shown in the 5 cases just mentioned, a roentgenogram which is normal except for some increase in bronchial markings is not incompatible with the existence of bronchiectasis.

Sinuses: Routine roentgen examination of the paranasal sinuses in all the cases studied revealed involvement in 27 cases. This high incidence of infection of the sinuses associated with bronchiectasis has received wide recognition in the literature.[9]

Bronchographic Findings.—Iodized poppyseed oil was injected in 30 of these 33 cases. Three children were too ill to permit its use. All 3 died. Permission for autopsy was not obtained, but in each case the suppurative nature of the illness, which probably consisted of both abscess and bronchiectasis, was obvious.

The bronchogram revealed bronchiectasis of the saccular type in 11 cases, of the cylindric type in 5 cases and of the combined saccular and cylindric type (with the saccular element predominant) in 5 cases. In 9 cases there were minimal or early changes, of either slightly cylindric or slightly saccular nature, while in 6 cases the bronchiectasis was associated with formation of an abscess. The lobes were involved as follows:

Lower lobe, left lung	16
Lower lobe, right lung	8
Middle lobe, right lung	6
Upper lobe, right lung	2
Upper lobe, left lung	2

In 4 of these cases two lobes were involved, and in 1 case the disease extended throughout the three lobes of the right lung.

It has been noted by many that the lower lobe of the left lung is the most frequent site of bronchiectasis. Duken and von den Steinen[10] attributed this selectivity to anatomic factors which produce mechanical obstruction more readily on the left than on the right. They stressed especially the fact that the right bronchus takes a more vertical course than the left bronchus and therefore is less angulated. However, the same circumstance which makes the right lung less susceptible to bronchiectasis due to obstruction makes it the site of predilection for accidents of aspiration. In 6 of 7 cases in this series bronchiectasis due to the latter cause occurred in the right lung.

9. Mullin, W. V.: The Accessory Sinuses as an Etiologic Factor in Bronchiectasis, Ann. Otol., Rhin. & Laryng. **30**:683 (Sept.) 1921. Webb, G. B., and Gilbert, G. B.: Bronchiectasis and Bronchitis Associated with Accessory Sinus Disease, J. A. M. A. **76**:714, (March 12) 1921. Schwartz, M., and Weiner, H. L.: Relationship of Chronic Bronchitis and Bronchiectasis to Paranasal Sinus Infection, Am. Med. **22**:623 (Oct.) 1927.

10. Duken, J., and von den Steinen, R.: Das Krankheitsbild der Bronchiektasie im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **34**:457, 1928.

Bacteriologic Findings.—The results of aerobic and anaerobic cultures of the sputums of 28 of these children and of cultures made from the sinus washings of 7 children are presented in table 2.

As in the experience of other observers, the bacteriologic findings revealed nothing conclusive. By way of emphasis, however, certain points may be reviewed. In nearly all the cases mixed cultures predominated, and there was a tendency for the bacterial flora to vary from time to time. No one organism or group of organisms was found uniformly, nor was there any apparent correlation between the severity of the disease and the bacterial findings.

Streptococci occurred most frequently, with the hemolytic form in almost 50 per cent of these cases, while there was a low incidence of fusospirochetal infection. Greey,[11] along with other investigators, found this same predominance of streptococci. As he pointed out, too much

TABLE 2.—*Bacteriologic Findings*

Organism	Culture of Sputum		Cultures of Material From Sinus
	Aerobic	Anaerobic	Aerobic
Streptococcus			
Viridans	24	..	..
Haemolyticus	16	..	..
Type not designated	..	5	..
Staphylococcus			
Aureus	15	..	1
Albus	3	..	4
Pneumococcus	11	..	1
Bacillus influenzae	5	..	..
Fusiform bacilli	6	8	..
Spirochetes	3	..	..
Unidentified cocci and diphtheroids	Small number	..	2
Sterile	..	..	4

stress should not be placed on this finding, because these organisms are common invaders with many infectious processes, and probably many types of bacteria are capable of destroying the structural integrity of the bronchi. However, it should be emphasized that most bacteriologic studies have been made in cases in which bronchiectasis has already developed and that the organism responsible for the antecedent pneumonia has not usually been known. It is possible, with the increasing recognition of those infections which predispose to the development of bronchiectasis in the majority of cases, that routine bacteriologic study of the earlier conditions may throw further light on the causative organisms. In connection with this, it may be well to cite our experience with the 6 patients seen during the illness which immediately preceded the onset of bronchiectasis. Pure cultures of pneumococci were recovered at the onset of the pneumonia in 3 of the 6 cases. Later cultures yielded no pneumococci but a mixed flora in which hemolytic streptococci pre-

11. Greey, P. H.: The Bacteriology of Bronchiectasis, J. Infect. Dis. **50**:203 (March) 1932.

dominated. In the remaining 3 cases a hemolytic streptococcus was the chief organism from the time of the first examination.

The few cultures of material from the sinuses were disappointing. Four were sterile, and in only 1 instance was an identical organism obtained from the sinus and from the sputum, the type XXVII pneumococcus.

DIAGNOSTIC CLASSIFICATION OF BRONCHIECTASIS

The physician having obtained as complete knowledge of a case as can be provided by the five means described for reaching a diagnosis, namely, history, symptoms, physical examination, roentgen study and bronchographic examination, it is extremely desirable that he make the diagnosis as informative as possible. It is as important to include the functional status of the lung along with the anatomic lesion in diagnosing suppurative pulmonary disease as it is in diagnosing heart disease. The following scheme has been found valuable:

I. Anatomic classification: description and location of lesion
   - A.—Minimal or early bronchiectasis (minimal cylindric and minimal saccular type and minor variations in bronchial contour)
   - B.—Cylindric bronchiectasis
   - C.—Saccular bronchiectasis

II. Functional classification:
   - A.—Dry—no symptoms
   - B.—Moderate symptoms
     1. Cough and expectoration of moderate severity
     2. Intervals of freedom from symptoms and signs
   - C.—Severe symptoms
     1. Cough and expectoration marked
     2. No intervals of freedom from symptoms and signs

The 33 cases in this series were classified according to this diagnostic scheme and analyzed further with a view to ascertaining the relation between the extent of the anatomic lesion and the clinical picture.

SACCULAR BRONCHIECTASIS

The cases of saccular and of saccular-cylindric type are considered in one group because, as might be expected from the existence of the saccular element in each variety, the history and the clinical course are similar with the two types. It is found that the cases fall into two divisions, those with severe symptoms and those with moderate symptoms. There are no cases of dry bronchiectasis unless one includes that of the boy (case 2) whose symptoms were severe for two or three years and then gradually improved, subsiding completely after ten years.

With Severe Symptoms.—The majority of the cases (11 of 16) fall into this classification. In these, cough and expectoration were marked and there were frequent bouts of fever. In many of these cases the condition has become progressively worse. With few exceptions the physical signs were extensive and persistent; usually they were those of chronic pneumonia. In no case did the roentgen shadow disappear, although variations within a certain range, dependent chiefly on the presence of a new flare-up, were common. In some cases the progression of the lesion was evidenced by the appearance of a new patch of infiltration. For example, in case 13 there was extensive saccular bronchiectasis of the lower lobe of the right lung. Within a few years a new focus, cylindric in type, was established in the lower lobe of the left lung. Unless the infection can be controlled, these cylindric dilatations will progress to the more serious saccular lesions present at the original site.

The etiologic history need not be repeated here, but I wish to draw attention to the fact that saccular bronchiectasis existed in all 5 cases of empyema with thoracotomy and that in 4 of these cases symptoms were severe. Without entering into a discussion of the many theories[12] concerning the interaction of fibrotic processes and associated bronchiectatic disease, one may conclude that pleurisy has an etiologic significance chiefly as a measure of the severity of the coexisting intrapulmonary infection which has resulted in bronchial destruction.

The prognosis in this group of cases is poor, the fate of the patients being one of increasing invalidism, although an occasional child attained a clinical cure, at any rate for a time (case 2). Four children have remained unimproved, 2 have died (1 of pneumonia, the other of osteomyelitis), and 4 had a rapid downhill course which necessitated surgical intervention. In 1 case this took the form of drainage by thoracotomy, which resulted in a clinical cure. In the other 3 cases lobectomy was done; the result was complete cure in 2 cases and considerable improvement in 1.

With Moderate Symptoms.—The remaining 5 cases of saccular and saccular-cylindric bronchiectasis fall into this classification. Expectoration and cough existed in moderate severity only, and fever was less frequent. The physical signs were less numerous and less likely to remain chronic or unchanged over a period of time than in the cases in which the symptoms were severe, nor were free intervals so unusual. In 4 cases the roentgen shadow was persistent. However, these shadows were not nearly so extensive as in the cases in which symptoms were

12. Staehelin, R.: Bronchiectasis, in von Bergmann, G., and Staehelin, R.: Handbuch der inneren Medizin, ed. 2, Berlin, Julius Springer, 1930, vol. 2, pt. 2, p. 1202.

severe. In the fifth case the roentgenogram was normal except for increased markings at the bases of the lungs, although the bronchogram showed saccular bronchiectasis of the lower lobe of the right lung and cylindric bronchiectasis of the lower lobe of the left lung.

The prognosis for the patients with moderate symptoms is definitely better than for those with severe symptoms. Three children have shown steady clinical improvement during a follow-up period ranging from five to twelve years, 1 child has been free from symptoms for seven years, and 1 child's condition has remained stationary. It might be said that the chances for intervals of improvement are greater the fewer the roentgen and the physical findings.

Prognosis.—In considering as a whole the group of cases of saccular bronchiectasis, it was found that the age of onset of the causative disease was no indication of the severity of bronchiectasis or the chances of clinical improvement. In following such cases carefully over a period of years one receives the impression that a certain clinical trend of severity or mildness is established in each case within a few years. This trend provides a basis for prognosis and is a valuable factor in determining the proper time for surgical intervention. In this series all the patients who showed appreciable improvement did so within a period of five years or less.

CYLINDRIC BRONCHIECTASIS

The 5 cases of cylindric bronchiectasis were subjected to a similar analysis. According to the diagnostic standards adopted, all fitted into the functional classification of moderate symptoms, with no cases in which symptoms were "severe" or "absent." Cough and expectoration were of moderate severity, with periods of relief, although no striking improvement could be noted in the general clinical course over several years of observation. The physical findings were definitely less conspicuous than in the cases of saccular type, being often inconstant and consisting mainly of rales over the involved area. Recurring episodes of pneumonia cleared completely but slowly as a rule. The only exception was found in case 20. Here the aspiration of a peanut produced a progressive suppurative lesion which undoubtedly was more extensive than indicated by the cylindric bronchial dilatations on the bronchogram. After three months of medical care, which included bronchoscopic drainage without improvement, permission for lobectomy was granted. Unfortunately the boy died of a postoperative abscess of the brain. Therefore, signs of persistent pneumonitis, often accompanied with those of cavitation, are much less likely to be present with cylindric than with saccular involvement. Apparently the ease with which the signs of pneumonic exacerbation clear is a good indication of the extent of the anatomic damage to the lung.

With respect to the roentgen findings, persistence of pulmonary shadows is as prominent a feature with the cylindric type of bronchiectasis as it is with the saccular type. However, here again there was 1 case in which roentgen examination showed nothing more than some increase in the basal bronchial markings, yet the bronchogram revealed a cylindric bronchiectasis of the lower lobe of the left lung. It may be stated at this point that in no case in this group was more than one lobe involved, whereas multiple lobar involvement occurred in 6 cases of the saccular type.

In many respects the clinical characteristics of cylindric bronchiectasis overlap those of saccular bronchiectasis with moderate symptoms, and this similarity of types applies also in the matter of prognosis. Generally speaking, the prognosis may be regarded as fair. All the children have enjoyed intervals of freedom from symptoms, and all have shown the same tendency to recurrent infections in the form of bronchitis or of pneumonitis. In 2 of these cases, however, the interval between acute episodes has lengthened appreciably.

In evaluating the prognosis of these cases some general considerations should be kept in mind. These children came from poor homes, their disease was often of long duration before medical attention was sought, cooperation in coming for regular intensive treatment was not always good, and fundamental hygienic principles were ignored. One cannot feel, then, that one has a fair index of the prognosis of these children as it would exist under ideal conditions, since most of these patients had been somewhat neglected. Certainly adequate medical measures, especially when applied soon after the onset of the disease, should result in improvement and a more hopeful outlook. The readiness with which one can attack the causative factors, the adequacy of drainage and the institution of specific procedures will determine the prognosis in the individual case almost as much as will the extent of the anatomic lesion.

THE GROUP WITH MINIMAL OR EARLY BRONCHIECTASIS

Here are included for analysis cases of 9 children (22 through 30) whose pulmonary damage according to the bronchogram was minimal. Injection of iodized poppyseed oil revealed slight but definite dilatations of the bronchi, 6 cylindric and 3 saccular. These changes not only were slight but were localized to an isolated group of small bronchi. The clinical course in these 9 cases offered confirmatory evidence of the slight nature of the anatomic damage. Three of these children (cases 26, 28 and 30) were admitted during their initial pulmonary infection. All suffered from severe, complicated pneumonia of duration varying from four to seven months. The first child (fig. 1*A* and *B*) had bilateral bronchopneumonia complicating measles, accompanied by pleurisy and

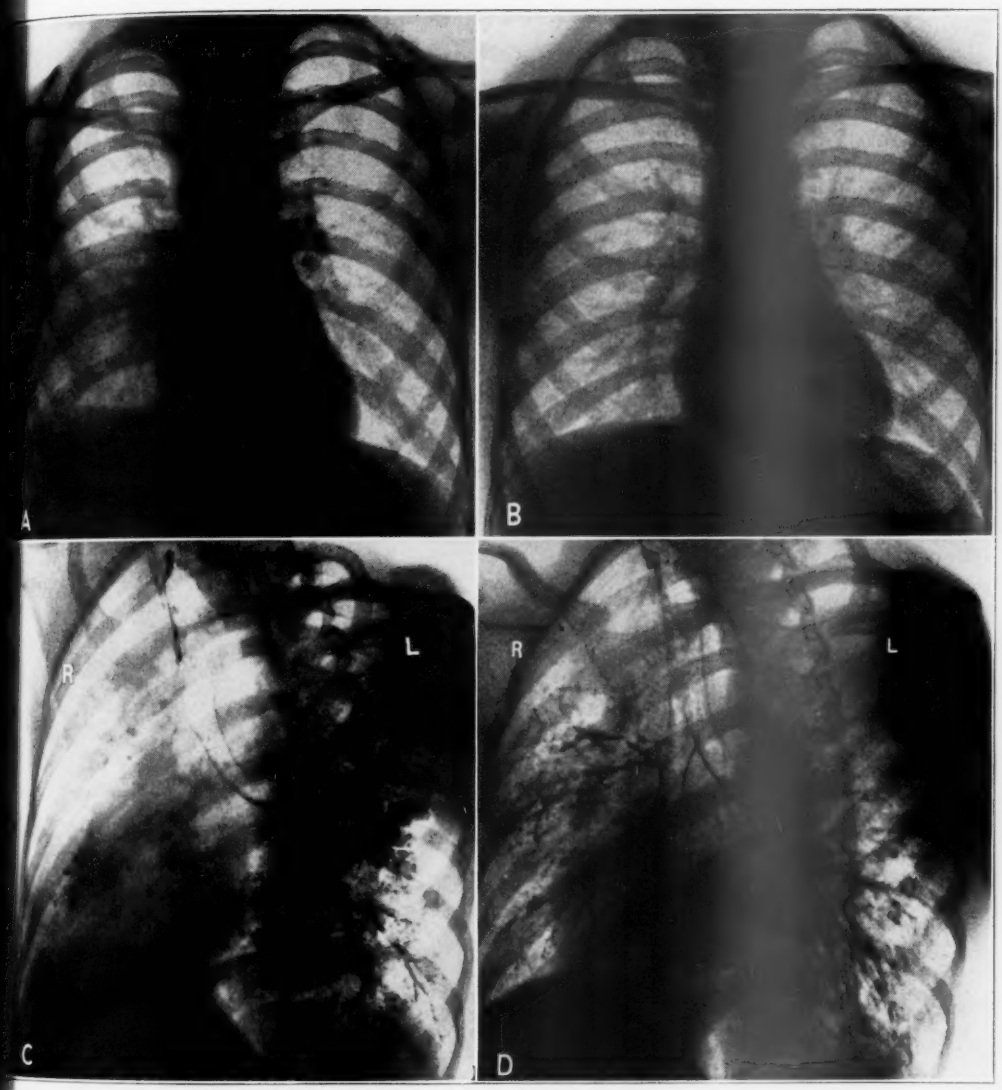

Fig. 1 (case 26).—*A*, roentgenogram in which is seen postmeasles bronchopneumonia with partial collapse of the right lung (elevation of the diaphragm, narrowing of intercostal spaces and slight retraction of the mediastinum to the right). Cyanosis was relieved by coughing and expectoration of thick sputum. *B*, roentgenogram showing complete clearing four months later (July 1933). *C*, first bronchogram (July 1933), showing small cylindric dilatations in the lower lobe of the right lung. *D*, second bronchogram, taken seven months later, showing entirely normal condition with no evidence of previous dilatations.

partial collapse of the lower lobe of the right lung and lasting four months. The second child (fig. 2*A* and *B*) had bilateral basal pneumonia which resolved only after six months. It was complicated by a small pleural effusion (10 cc. of turbid fluid obtained on tap) and by collapse of the lower lobe of the right lung. The third child contracted

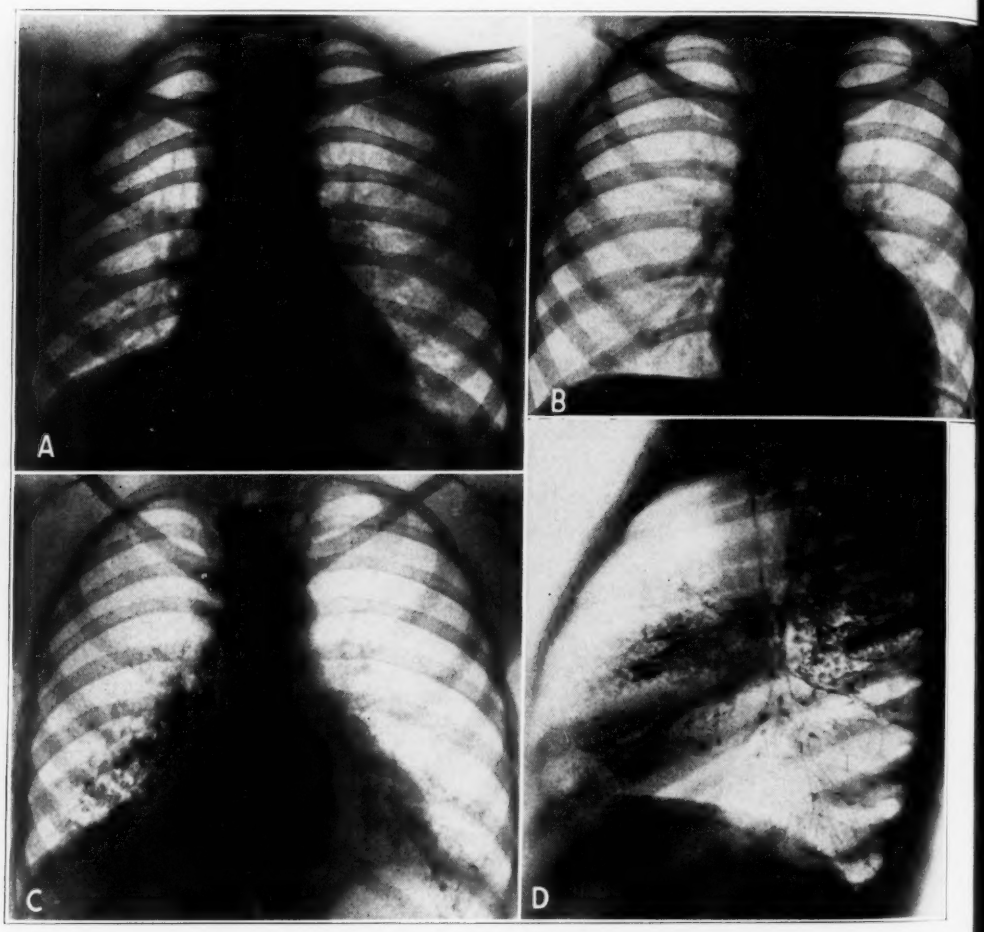

Fig. 2 (case 28).—*A*, bilateral basal bronchopneumonia; collapse of the lower lobe of the right lung is indicated by the triangular shadow. *B*, normal roentgenogram taken six months later. The triangular shadow at the base of the right lung has disappeared. *C*, the first bronchogram (March 1933). Cylindric dilatations were revealed by the injection of iodized poppyseed oil before complete inflation of the lower lobe of the right lung had taken place. *D*, the second bronchogram (December 1933), showing the lateral view. The cylindric dilatations have been replaced by normal bronchial contour, after resolution of the pneumonia and complete reexpansion of the lower lobe of the right lung. For purposes of reproduction the outline of the bronchi has been retouched to show normal bronchial contours.

pneumonia with partial collapse of the lower lobe of the right lung following a post-tonsillectomy abscess. Resolution took place after seven months. Cough and expectoration of considerable amounts (2 to 13 ounces [59 to 384 cc.]) were the chief symptoms, with hemoptysis and cyanosis occurring in the first case. Treatment was conducted along the following lines: Adequate drainage, by posture and by use of the bronchoscope, was instituted as soon as the acute phase of the pneumonia had subsided. Absolute bed rest was imposed until complete disappearance of all evidence of infection, including fever, physical signs and roentgen shadows. Sinusitis in 2 of these children was treated by the use of nasal drops of epinephrine hydrochloride in a 1:8,000 dilution, and tonsillectomy was performed for 1 child as soon as the general condition permitted. On bronchoscopic examination, pus was seen coming from the involved bronchi, and seven bronchoscopic examinations were made of the first child, twelve of the second and nine of the third before this purulent exudate ceased. The results have been most gratifying. During follow-up periods ranging from one to four years these children have enjoyed good health except for minor colds, common among children, and have had no pulmonary recurrences.

In the remaining 6 cases the initial causative illness had taken place at sometime in the past. One boy has remained free from symptoms since the removal of a nail from the bronchus; while 1 boy came under observation because of hemoptysis, which subsided with rest in bed. He has had no other symptoms. The other 4 children have been treated for their intercurrent colds and attacks of pneumonitis by the methods just cited. Marked improvement has taken place, as shown by the decreasing frequency as well as the diminishing severity and duration of exacerbations. Thus the results in these cases have also been satisfactory, but not to the same extent as in the 3 cases of early bronchiectasis which were described first. The greatest good results from intensive treatment during the initial pneumonia, for this is the infection which paves the way to chronic and increasing disease.

It is obvious, therefore, that this group with minimal involvement has a much better prognosis than the groups with the saccular and the cylindric type. Chronicity of all manifestations, so characteristic of saccular and of cylindric bronchiectasis, is not a feature of minimal bronchiectasis. The tendency of symptoms, physical signs and roentgenograms is to clear, with recurrences taking a milder form. Nor are clinical cures unusual, as indicated by the cases of 4 of the 9 patients, who have remained well for several years.

That a chronically bronchiectatic lung cannot be restored to normal structure and function needs no comment, but that such restoration may take place in the early stages of bronchiectasis, especially in young children, is conceded as a distinct possibility by many observers.

Erb [13] wrote: "The appearance of the bronchi in the early stages of bronchiectasis before relining with epithelium takes place is such as to suggest that healing at this stage with actual diminution in size of the bronchi may be promoted by bronchoscopic drainage. When once the bronchi become relined with epithelium, such healing is no longer possible." In the publication by Duken and von den Steinen [10] reference was made to the ability of the lung in young children to repair itself and also to the growth factor which compensates for the destructive processes by the development of new, healthy tissues. Likewise Miller [14] stated:

> Considering the great frequency of such pulmonary infections (the bronchopneumonias associated with measles and pertussis) in childhood, it is astonishing that their chronic sequelae resulting in bronchiectatic disease are not more frequently found in clinical practice. This probably can be explained by the fact that the lungs of children are still in their developmental phase, and by virtue of their continued growth, they may be capable of restitution and elimination of destructive processes which on first impression might seem irreparable.

The high percentage of clinical cures in my own series (4 of 9 cases), especially in the children treated adequately during the initial pulmonary infection, has caused me to view favorably the possibility of complete anatomic and physiologic repair. The demonstration of such repair must depend perforce on the repeated use of iodized poppyseed oil in the individual case in order to trace the course of the lesion. The ideal program would include a periodic bronchographic examination to ascertain whether the changes in bronchial structure are transitory, permanent or the beginning of a more progressive damage. Such a program naturally offers practical difficulties inherent in the character of the average clinic population. I have been able to obtain repeated bronchograms for 4 children. In case 26 the second bronchogram showed a normal bronchial tree, in contrast to the small cylindric changes seen in the first bronchogram, taken seven months previously (fig. 1 *C* and *D*). In case 28 bronchograms showed a similar return to normal bronchial structure. In figure 2 *C* are seen the cylindric dilatations in the right lower lobe present before complete resolution and expansion, while in figure 2 *D*, which shows a plate taken nine months later, it is possible to trace the normal ramifications of the bronchial tree (demonstrated best in the lateral view). The findings in these 2 cases illustrate the occurrence of anatomic as well as clinical cures of early minimal bronchiectasis. It is not unreasonable to assume that if these children had not received such intensive treatment they would have joined the

13. Erb, I. H.: Pathology of Bronchiectasis, Arch. Path. **15**:357 (March) 1933.

14. Miller, J. A.: The Pathogenesis of Bronchiectasis, J. Thoracic Surg. **3**:246 (Feb.) 1934.

ranks of those who return months or years later because of impaired health and a productive cough dating from this initial attack of pneumonia.

In case 21 is demonstrated another possible outcome of bronchial damage in children. In a 1 year old infant the middle lobe of the right lung collapsed in 1932 as a result of obstruction by enlarged tuberculous lymph nodes (fig. 3 *A* and *B*). Shortly thereafter the patient contracted type XIV pneumococcic bronchopneumonia, from which he made a slow recovery. In 1934 the persistent collapse of the middle lobe of the right lung and the antecedent history of pneumonia suggested the possibility of bronchiectasis, which was confirmed by the introduction of iodized poppyseed oil (fig. 3 *C*). Two bronchoscopic examinations at this time revealed a profuse purulent discharge coming from the lower part of the right main bronchus. During the past three years, i. e., 1934 to 1937, the child has had intermittent care in a sanatorium. At such times as he has returned to Bellevue Hospital, he has had signs of recurrent bronchitis with every infection of the upper respiratory tract. However, his general condition has steadily improved, and his roentgenograms have shown gradual reexpansion of the affected lobe until evidence of collapse is no longer visible. Calcifications are now seen in the hilar region on the right (fig. 3 *D* and *E*). A bronchogram taken in 1937 (fig. 3 *F*) showed the continued existence of bronchial dilatations, but they were definitely less extensive in proportion to the increased size of the lung. Two interesting features are illustrated in this case: First, reexpansion of a lobe may take place, even when its collapse has persisted for several years, despite the occurrence of inflammatory changes within that lobe. Second, the growth factor may minimize the effects of bronchiectasis which occurs early in life. In the case just described, cylindric bronchiectasis at first involved the major part of the middle lobe of the right lung. At present the condition involves only a portion of the lung, and in time it may become limited to an extremely small area. According to Nobécourt [15] and other writers already quoted, as the lung grows the affected bronchi ultimately come to have normal or nearly normal proportions.

The last of 4 cases in which the bronchogram was repeated concerned a 10 year old girl (case 27), who first came under observation during an episode of recurrent pneumonia. She had suffered a series of attacks since the age of 5 years, when measles, pertussis and pneumonia developed in rapid succession. A bronchogram demonstrated minimal cylindric bronchiectasis in the lower lobe of the left lung. There was no change in the findings of a second bronchogram, taken eight months

15. Nobécourt, P.: Bronchopneumonies subaiguës et chroniques avec bronchiectasies, in Précis de médicine infantile, ed. 5, Paris, Masson & Cie, 1926, p. 385.

later. Under therapeutic measures already described, the patient has shown remarkable clinical improvement, which has extended over a five year follow-up period. It is planned to repeat the bronchogram a third time if possible; yet one may hazard a guess that there will be no appreciable change in the existent dilatations. Such a conjecture is based on two features of the case. The first is the long-standing history of repeated damage by recurrent pneumonic infections before the condition was recognized. The second is the fact that the patient is in late

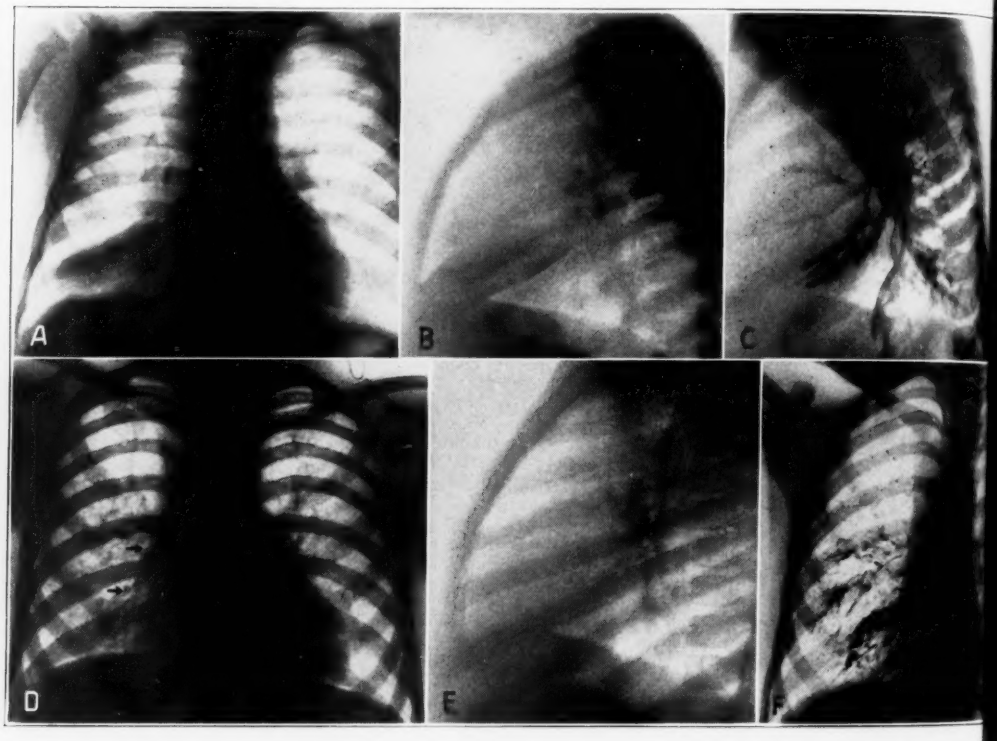

Fig. 3 (case 21).—*A* and *B* reveal collapse of the middle lobe of the right lung in a 1 year old infant (1932), the result of pressure by enlarged tuberculous tracheobronchial lymph nodes. *C*, the first bronchogram, taken in 1934. Instillation of iodized poppyseed oil showed the presence of cylindric bronchial dilatations in the still collapsed middle lobe. *D* and *E* (1937) show areas of calcification at the hilar region on the right. There has been complete reexpansion of the middle lobe of the right lung. *F*, the second bronchogram (1937). Bronchial dilatations persist but occupy a smaller portion of the expanded and growing middle lobe.

childhood, when the favorable influence of rapid growth on the reparative powers has begun to diminish. Emphasis is placed on cases of minimal or early bronchiectasis because on its recognition depends the prevention, in many cases, of frank bronchiectasis in childhood. Much

clinical and pathologic evidence is presented in the literature[16] in support of the conception that bronchiectasis is more often a progressive, slowly developing disease than an acute one. The final, chronic stage represents the culmination of the effects of intermittent infection of the respiratory tract over a period of years on these early initial lesions. It follows that in order to decrease the incidence of advanced bronchiectasis it is essential to suspect that in every case prolonged pneumonia threatens the functional and structural integrity of the bronchi and to counteract such destructive influences by intensive and persistent treatment in the early stages.

When one correlates and summarizes the results of the analysis of the three main types of bronchiectasis, namely, the saccular, the cylindric and the minimal, it becomes apparent that the clinical picture is an index of the extent of the anatomic damage. In other words, the more severe the clinical picture the more extensive the degree of bronchiec-

TABLE 3.—*Correlation Between Diagnostic Criteria and the Anatomic Status*

	Saccular Bronchiectasis (Including Saccular Cylindric)	Cylindric Bronchiectasis	Minimal Bronchiectasis
Symptoms	Severe Chronic	Less severe Free intervals possible	Free intervals usual Recurrences mild Complete clearing possible
Physical signs	Extensive Persistent	Less extensive Free intervals possible	Free intervals usual Recurrences mild Complete clearing possible
Roentgenogram	Persistent shadow	Persistent shadow	Absence of persistent shadow
Bronchogram	Single or multiple lobe involvement	Limited to one lobe	Limited to one lobe, often to small group of bronchi
Prognosis	Poor	Fair	Good

tasis. The diagnostic criteria on which this clinical picture is evaluated are represented briefly in table 3.

The prognosis must be based on a knowledge of both the anatomic and the functional status. It is bad in cases in which symptoms are severe, especially if the lesion is saccular. It is better in cases in which symptoms are moderate, especially if the lesion is cylindric. It is best in those in which there are slight anatomic lesions of limited pulmonary involvement. The readiness and frequency with which freedom from acute exacerbations occurs make for a better prognosis, while any marked involvement of the pleura makes for a worse prognosis. The duration of illness must also be stressed, for the longer the condition has existed the less favorable the outlook.

16. (*a*) Riviere, C.: Damaged Lungs and Bronchiectasis, Brit. M. J. **1**:141 (Jan. 27) 1923. (*b*) Jameson, H. P.: Remote Prognosis of Pneumonia, Arch. Dis. Childhood **4**:365 (Dec.) 1929. (*c*) Davidson, M., and Pearson, W. J.: Chronic Lung Infections in Children, Am. J. Dis. Child. **33**:1 (Jan.) 1927. (*d*) McNeil, C.; MacGregor, A. R., and Alexander, W. A.: Studies of Pneumonia in Childhood: Bronchiectasis and Fibrosis, Arch. Dis. Childhood **4**:170 (Aug.) 1929. Duken and von den Steinen.[10] Erb.[13]

THE GROUP WITH POTENTIAL BRONCHIECTASIS

This detailed study emphasized the factors concerned in the etiology and pathogenesis of bronchiectasis and pointed the way to the early recognition of involvement. Interest then extended still further. Can the disease be prevented by finding a clinical picture which may precede even the beginning of bronchial destruction? To answer this question attention was directed to another group of children who were being followed in the chest clinic. These children included those who sought relief for frequent infection of the respiratory tract of one form or another, and as sinusitis was being studied at the time a large number of cases were collected. The principal roentgen findings consisted of increased radial streakings, especially at the bases, and, during acute exacerbations, of pulmonary infiltrations of varying degrees which cleared with subsidence of the attacks. The possibility of bronchiectasis had not been considered in these cases because the classic textbook picture was thought of as essential to the diagnosis,. However, with interest in bronchiectasis aroused, the value of these cases at once assumed special significance. It was decided to subject these cases to the same analysis applied to the cases of bronchiectasis, with the object of determining points of similarity and difference. Fifty-two cases in which data were sufficient to make them suitable for study were chosen. The term potential bronchiectasis has been applied to this group, using again a term suggested by the classification of heart disease.

DIAGNOSTIC CRITERIA

History.—Forty-one children, or 78 per cent, gave a history of pneumonia, either as a single attack or, more often, as multiple attacks. Of these 41 patients, 24 dated their respiratory complaints to this disease. Although in 6 there was an accompanying plastic pleurisy, in no case was there frank empyema. In the majority of cases the pneumonia occurred in children under 5 years of age, with a particularly high incidence in the first 2 years of life. In 2 of the 24 cases the pneumonia was a complication of measles, and in 2 others it was a complication of pertussis.

Bronchitis was noted in the histories of 35 patients; it was usually recurrent. In 13 cases these attacks of bronchitis had begun in infancy.

In 4 children pertussis marked the onset of their symptoms, with complicating pneumonia present in 2 cases, as just stated.

Measles was cited as the cause of chronic illness in 2 instances, but in both it was followed by pneumonia.

Colds, with symptoms referable to involvement of the upper respiratory tract, were almost universally present (49 of the 52 cases).

The high incidence of infections of the respiratory tract both of the upper air passages and of the lungs, with a marked tendency to recur-

rence, is impressive. To appreciate better the importance of this type of history to subsequent findings in this analysis, a control group of 361 cases was studied with the object of ascertaining the incidence of pneumonia, measles and pertussis in the general population of the clinic. Roentgenograms had been taken in these cases for conditions other than recurrent infections of the respiratory tract; the group included chiefly children under observation for positive Mantoux reactions. All the roentgenograms were normal, with no evidence of fibrosis or increase in interstitial pulmonary markings.

The importance of these three diseases, pneumonia, measles and pertussis, as responsible factors in chronic illness of the respiratory tract is well recognized. Their incidence in both the cases of bronchiectasis and those of potential bronchiectasis is striking. The incidence of these diseases in the general population, as represented by this control group, who had normal roentgenograms, is given in table 4.

TABLE 4.—*Incidence of Pneumonia, Measles and Pertussis*

	Control Group, Percentage	Group with Potential Bronchiectasis, Percentage	Group with Bronchiectasis, Percentage
Pneumonia	33	78	67
Measles	74	74	91
Pertussis	44	62	46

It can readily be seen that there is a marked difference in the incidence of pneumona in the groups with potential and with actual bronchiectasis as compared with that in the control group, being notably higher in the former case. On the other hand, little can be deduced from a comparison of the incidence of measles and pertussis in the three groups other than evidence of the high morbidity of these diseases. However, it may be recalled at this point that measles was not a causative factor in any instance unless it was complicated by pneumonia. With regard to pertussis, probably the same association of the disease with pneumonia or bronchitis holds true, even though the patient's statement includes simply an admission of pertussis. The basis for this assumption is the pathology of the disease and the fact that medical supervision is not always sought during its course. In other words, bronchopulmonary infections, either primary or secondary to measles or pertussis, play a highly significant role in the production of varying grades of chronic respiratory illness.

Principal Symptoms.—Forty-five of the 52 patients complained of cough. However, this cough occurred only in the acute attacks of illness and subsided completely between exacerbations, as a rule. The other important symptom, expectoration, was present in only 11 cases, and it also showed the tendency to clear between acute attacks.

Principal Physical Signs.—Signs of bronchitis, when present, disappeared quickly, with one exception; in this case a boy had severe sinusitis and bronchitis for four months. Signs of pneumonitis also cleared completely, and although in the majority of cases this clearing took place within a short time, there were several cases in which it was prolonged.

Sinusitis.—Both clinical and roentgen evidence of infection of the sinuses existed in 48 of the 52 cases. This corresponds to the high incidence of sinusitis in the cases of bronchiectasis. Just what role sinusitis plays in relation to bronchiectasis need not be discussed here. Suffice it to say that it is found in the majority of children who have chronic pulmonary symptoms and that treatment of the sinuses results in improvement in many cases, perhaps by lessening the tendency to renewed infections.

Roentgen Findings.—Roentgen observation of patients with pneumonia revealed shadows at one or both bases of the lungs; these cleared completely in every instance, although the rate of clearing varied, being slow in some cases and rapid in others. In the intervals free from pneumonic exacerbations the roentgenograms in all 52 cases showed a definite increase in the bronchial markings at the bases; this was especially prominent in the region adjacent to the right cardiac border and in the retrocardiac space as seen laterally. For convenience in study, the extent of fibrosis, as represented by these heavy bronchial markings, was arbitrarily indicated as 1 plus and 2 plus. Numerous roentgenograms made in all these cases over an extended period of observation made it possible to discount transitory changes resulting from current infections and to ascribe to each patient the degree of fibrosis which seemed most constant for him over a number of years.

In studying the relation of the degree of fibrosis to the age incidence of pneumonia, measles and pertussis, it was found that the younger the patient when one or a combination of these illnesses occurred the more marked the fibrosis. It was also noted that when a child had more than one of these three diseases the rapidity with which one followed the other also determined the degree of fibrosis. That such damage to the lung as was indicated by the presence of bronchial scars on the roentgenogram does not always result was shown clearly by the control group. The roentgenograms of these patients were entirely negative, even though the histories revealed in many cases the occurrence of these three diseases either singly or in combination and frequently early in life. In other words, patients whose symptoms date from an antecedent attack of pneumonia are likely to show evidence of it by an increase in the bronchial markings, while those with no symptoms after pneumonia are likely to have negative roentgenograms.

Bronchographic Findings.—The injection of iodized poppyseed oil in 17 of these 52 cases revealed normal bronchial structures in each one.

COMPARISON OF DIAGNOSTIC CRITERIA OF THE GROUP WITH POTENTIAL AND OF THE GROUP WITH ACTUAL BRONCHIECTASIS

Of the major symptoms, cough was an outstanding complaint in both these groups, but it tended to be constant in the group with bronchiectasis whereas it cleared completely between acute attacks in the group with potential bronchiectasis. The presence of expectoration, however, was definitely more characteristic of the former than of the latter group. It appears that the production of sputum indicates the progression of a pathologic status of which cough is the first indication.

Both groups may have similar pulmonary findings of either pneumonitis or bronchitis. The point of differentiation between the two lies in the rapidity and completeness of resolution. With bronchiectasis there is a greater tendency to chronicity and slow disappearance of physical signs. Another difference lies in the distribution of the bronchitis, which is often generalized in the group with potential and localized in the group with actual bronchiectasis.

The same observation as to chronicity can be made concerning the roentgen findings. In the cases of potential bronchiectasis in which infiltrations were evident, these disappeared completely although not necessarily rapidly. In the cases of bronchiectasis they were frequently persistent. Fibrosis, as indicated by the accentuation of bronchial markings, was present as the only roentgen evidence of bronchiectasis in a relatively small percentage of cases, whereas it was the single outstanding feature of the group with potential bronchiectasis.

In general, then, the two groups shared identical findings at certain stages, and they differed chiefly in their capacity to recover from acute exacerbations. As long as each group maintains its most striking characteristics, it is relatively simple to recognize typical potential and typical actual bronchiectasis. But somewhere the two groups merge gradually, and the clinical similarity becomes such as to make impossible a differential diagnosis without the use of iodized poppyseed oil. These borderline cases are coming to our attention with increasing frequency; their importance is stressed by several writers, among whom may be mentioned Armand-Delille,[1] Duken and von den Steinen[10] and Miller.[14] The 2 cases presented in table 5 show that identical clinical findings may be present without anatomic changes in the bronchogram. The functional capacity in both was impaired, even though the pathologic process had advanced a step further in one than in the other.

In connection with these 2 cases it seems appropriate to refer to a case described by Duken and von den Steinen[10] in which there was

transition from borderline involvement to actual bronchiectasis under the influence of repeated infections. The report concerns a child with continual attacks of bronchitis on the right side. The first bronchogram was normal. The second, repeated fifteen months later, showed definite slight dilatations of the terminal bronchi of the lower lobe of the right lung.

PATHOGENESIS

A review of the many factors responsible for the production of bronchiectasis indicates that pneumonia, either primary or secondary to measles or pertussis, leads by far in frequency of occurrence. The incidence of these particular infections has been shown to be equally high in the cases of potential bronchiectasis and to result in the same

TABLE 5.—*Comparison of Findings in a Case of Potential and a Case of Minimal Bronchiectasis*

	Case J. M.	Case 29 (table 1)
History	Recurrent bronchitis and pneumonia at base of left lung since initial pneumonia at 5 years	Recurrent bronchitis and pneumonia at base of left lung since initial pneumonia at 1 year
Symptoms	Fever, cough, expectoration with acute exacerbations; slow, complete clearing (average several weeks); well in intervals	Same as for J. M.
Physical signs	Slowly resolving pneumonia with complete clearing	Same as for J. M.
Roentgenograms	Slow, complete clearing of infiltration in L. L. L.	Same as for J. M.
Sinuses	Diseased	Same as for J. M.
Bronchogram	Negative	Minimal cylindric bronchiectasis in L. L. L.
Diagnostic classification	Potential bronchiectasis (borderline)	Minimal cylindric bronchiectasis with moderate symptoms

sequelae of disorders of the respiratory tract. The *type* of history then is the same. Such differences as exist between the two groups can be attributed to the *severity* of this history. Further analysis of this history of infection reveals that obstruction is often a contributory element in the pathogenesis of bronchiectasis. In fact, obstruction accompanied infection in all 6 cases of bronchiectasis observed during the initial illness (table 1, cases 7, 14, 21, 26, 28, 30). Five cases have been selected (including 4 of those just cited) to demonstrate the stages in the evolution of potential into actual bronchiectasis by a variation in the severity of these two factors of infection and obstruction. They are presented in table 6.

Briefly, the table illustrates the increasing damage to the bronchial structures as the two elements of pulmonary infection and obstruction become more serious in nature and longer in duration. In the first 3 cases obstruction from acute inflammatory changes resulted in collapse

TABLE 6.—*Pathogenesis of Bronchiectasis: Analysis of Five Cases Observed During Initial Pneumonia, Presented in Order of Increasing Severity*

TABLE 6.—*Pathogenesis of Bronchiectasis; Analysis of Five Cases Observed During Initial Pneumonia, Presented in Order of Increasing Severity*

	Case of R. M.	Case 26	Case 28	Case 21	Case 14
Age	10 years	5 years	6 years	1 year	4½ years
Previous history	Frequent colds	No illness	No illness	No illness	No illness
Present illness	Bronchopneumonia L.L.L. and R.L.L. with collapse R.L.L.	Measles, bronchopneumonia L.L.L. and R.L.L. with partial collapse of R.L.L.; pleurisy on right	Bronchopneumonia L.L.L. and R.L.L. with collapse R.L.L.; pleurisy on right	Collapse R.M.L. secondary to tuberculous nodes and bronchopneumonia	1st pneumonia, 2d pneumonia, and 3d pertussis-pneumonia within 6 weeks; collapse of left lung
Symptoms	Fever, cough, foul sputum (1 oz. daily), cyanosis	Fever, cough, blood-tinged sputum (13 oz. daily), cyanosis	Fever, cough, sputum (4 oz. daily)	Fever, cough, no sputum (too young), cyanosis	Fever, cough, foul sputum (24 oz. daily)
Physical signs	Consolidation, cavitation R.L.L. > L.L.L.	Consolidation right base; rales left base; pleurisy (dry tap)	Consolidation → cavitation R.L.L.; consolidation L.L.L.; pleurisy (10 cc. turbid fluid)	Shifting consolidation L.L.L. → R.L.L. → L.L.L.	Consolidation and cavitation of left lung
Roentgenograms	Figure 4 *A*	Figure 1 *A*	Figure 2 *A*	Figure 3 *A* and *B*	Figure 5 *A*
Sinusitis	Right antrum; right frontal sinus; atrophic rhinitis	Both antrums	Pansinusitis	No involvement	Both antrums; ethmoid sinuses on right
Sputum culture	Streptococcus viridans, pneumococcus, Staphylococcus aureus, gram-negative fusiform bacilli	Streptococcus haemolyticus, Str. viridans, staphylococcus, gram-negative fusiform bacilli	Pneumococcus (type I), Str. haemolyticus, Staph. aureus, gram-negative fusiform bacilli	Pneumococcus (type XIV); 1 year later streptococci, Staph. aureus, gram-negative fusiform bacilli	Str. haemolyticus, Staph. aureus, gram-negative fusiform bacilli
Duration of illness	Symptoms, signs, roentgen findings: complete clearing in 3 months	Symptoms, signs, roentgen findings: complete clearing in 4 months	Symptoms, signs, roentgen findings; complete clearing in 6 months	Acute phase 1 month, followed by chronic clinical course	Acute phase 6 weeks, followed by chronic clinical course
Treatment	Bed rest 3 months; sinus drainage; postural drainage; bronchoscopic drainage (3 times)	Bed rest 4 months; sinus drainage; postural drainage; bronchoscopic drainage (7 times); tonsillectomy	Bed rest 6 months; sinus drainage; postural drainage; bronchoscopic drainage (12 times)	Inadequate bronchoscopic drainage (2 times); treated in sanatorium for tuberculous patients	Uncooperative; left hospital against advice
Bronchogram	Negative (figure 4 *C*)	Minimal dilatations R.L.L. (figure 1 *C*)	Minimal cylindric bronchiectasis R.L.L. (figure 2 *C*)	Cylindric bronchiectasis R.M.L. (figure 3 *C*)	Saccular and cylindric bronchiectasis L.U.L. and L.L.L. (figure 5 *B*)
Period of follow-up	3 years	4 years	1 year	5 years	5 years
Condition	Entirely well (figure 4 *B*)	Entirely well; second bronchogram negative (figure 1 *B* and *D*)	Entirely well; second bronchogram negative (figure 2 *B* and *D*)	Recurrent bronchitis; roentgenogram, gradual reexpansion R.M.L.; second bronchogram, less extensive bronchiectasis (figure 3 *D*, *E*, *F*)	Recurrent pneumonia; roentgenogram unchanged (i. e., contracted left lung) (figure 5 *C*)

of a lobe and was relieved with subsidence of the pneumonic process. R. M. had the shortest clinical course and recovered with no evidence of bronchiectasis (fig. 4 *A, B* and *C*). The illness in case 26 was more prolonged, and studies with iodized poppyseed oil revealed slight transitory bronchial dilatations (fig. 1). In case 28, in which the clinical course was longest, there developed minimal cylindric bronchiectasis, which also proved transitory (fig. 2). In the fourth case (case 21, fig. 3) obstruction was the predominant element. Evidence of bronchostenosis by tuberculous nodes was present prior to the onset of pneumonia. Because of the slow healing characteristic of tuberculosis, rapid reexpansion of the collapsed infected lobe was impossible, and the deleterious effects of interference with drainage, prolonged over several years, were manifested by the resultant marked cylindric dilatations of the bronchi. The fifth case (case 14, fig. 5 *A, B* and *C*) showed the effect of overwhelming infection in the production of acute bronchiectasis. Three attacks of pneumonia and pertussis in close succession brought about rapid widespread saccular destruction of the small bronchi of the entire left lung. The initial collapse was probably the result of bronchial stenosis by inflammatory exudate and possibly by enlarged congested lymph nodes. With the persistence of the infective processes this collapsed lung has been converted into a permanently contracted bronchiectatic mass, in which further disintegration of bronchial structures is undoubtedly taking place.

In these 5 cases has been demonstrated, step by step, the clinical path by which alteration in severity and in duration of infection and obstruction results in progressive destruction of the bronchial walls. Beginning in the relatively normal bronchi of the child with potential involvement, the changes progress to intermediate disturbances of minor and often transitory nature and finally to definite permanent dilatations characteristic of cylindric and saccular bronchiectasis. A corresponding succession of changes from initial lesion to end stage was demonstrated pathologically in the excellent articles by Erb [13] and by McNeil and his co-workers.[16d]

The influence of intensive treatment in the initial phases in determining the end result of these pulmonary infections must not be ignored. Thorough treatment in the first 3 cases undoubtedly checked inflammatory processes which would have paved the way for recurrent infections and progressive structural damage.

SUMMARY AND CONCLUSIONS

A series of cases in which histories showed prominent disturbances of the respiratory tract have been studied according to gradations of descending severity in order to point out the fundamental principles involved in the diagnosis, pathogenesis and prevention of bronchiectasis.

Infection and obstruction seem to play the chief role in the production of anatomic and physiologic pulmonary damage. This damage may be of such severity as to result in acute bronchiectasis. More frequently it results in a low grade chronic inflammation of the bronchi which renders them less resistant to subsequent bacterial invasion.

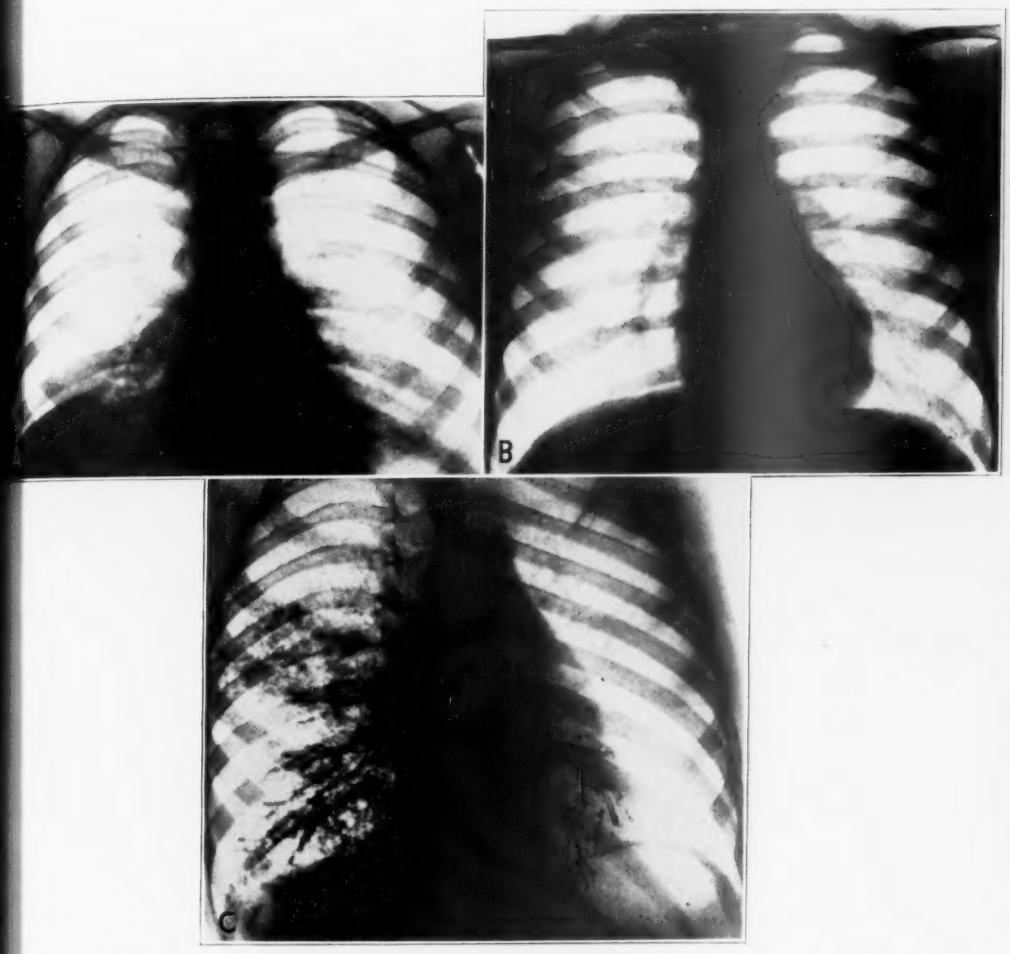

Fig. 4 (case of R. M.).—*A*, bilateral basal bronchopneumonia with a triangular shadow at the base of the right lung due to collapse of the lower lobe. *B*, roentgenogram made three months later, after complete clinical recovery. Note the disappearance of the state of collapse and of pulmonary infiltrations. *C*, bronchogram taken after recovery, showing no evidence of bronchiectasis.

Eventually bronchial dilatations may develop unless proper remedial measures are instituted. The recognition of this subacute pathologic state, with its far reaching possibilities, deserves particular stress and has

led to the clinical description of the case of potential bronchiectasis. The sequence of events in the evolution of bronchiectasis may be represented schematically as in figure 6.

The use of iodized poppyseed oil is of invaluable assistance in determining the exact nature of bronchial dilatation. However, its limitations must be emphasized. The bronchogram does not reveal

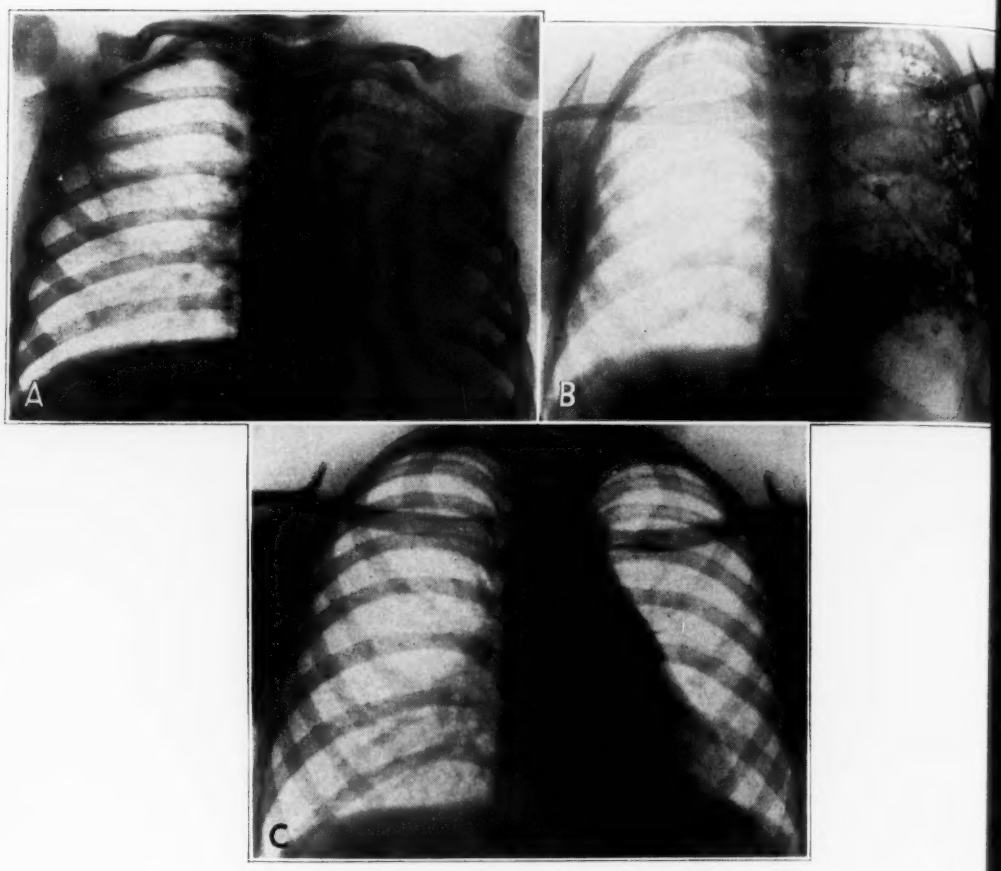

Fig. 5 (case 14).—*A*, roentgenogram taken in 1932, showing pneumonic infiltration of the entire left lung, with collapse; there is retraction of the mediastinum to the left. *B*, bronchogram made with iodized poppyseed oil in 1932. Saccular and cylindric bronchiectasis involves particularly the peripheral portions of the bronchi of the lower lobe of the left lung and, to a less extent, of the upper lobe. *C*, made in 1937, shows permanent retraction of the mediastinum due to fibrosis and bronchiectasis of the left lung.

degrees of fibrosis or functional insufficiency of damaged mucous glands,[10] which may readily result in impaired health. This is well illustrated by the patients with potential, borderline bronchiectasis.

whose bronchograms are negative but whose state of invalidism is identical with that found in children who have definite bronchiectasis. Findings obtained with iodized poppyseed oil should therefore not be made the absolute criterion of damage to a lung or of the need for treatment. In the final analysis, the determining factor must be the functional capacity of the lung, even when anatomic changes cannot be demonstrated clinically.

It has been shown that the amount of damage to the lung is reflected in the clinical course. The transition from the potential stage to the end stage of chronic bronchiectatic disease is accompanied by progression in the severity of the symptoms and in the physical and roentgen findings. Attention is drawn to the closeness with which the symptoms of potential borderline involvement may simulate those of bronchiectasis.

The prognosis of well established bronchiectasis is admittedly discouraging, even though recent surgical advances offer a new hope to

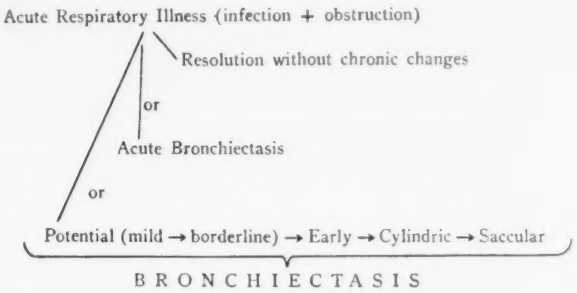

Fig. 6.—Diagram showing the evolution of bronchiectasis.

those victims in whom no improvement can be expected from medical care. The intelligent approach to the problem of bronchiectasis, however, must be made through the recognition of those conditions which predispose to its development. Encouraging results can be expected by diligent investigation and care of the child with recurrent or chronic symptoms of involvement of the respiratory tract, even when early bronchial dilatation has already taken place. Even more can be accomplished by thorough treatment of every attack of pneumonia which is prolonged or which is preceded by measles or pertussis. Such treatment includes the continuance of rest in bed, not only until the febrile period has subsided but until the physical signs and the roentgenogram have completely cleared. It includes the institution of proper pulmonary drainage by posture and, if necessary, by bronchoscopic treatment. As these measures are taken, foci of infection in the sinuses and tonsils must be eradicated, for these enhance the opportunities for recurrent illness. In the subsequent care of the child, general hygienic measures cannot be too strongly stressed. Sufficient rest and a properly balanced

diet with a high vitamin content are important. Meticulous care must be exercised in avoiding exposure to infections and in treating promptly even a mild cold. Of most practical value would be the establishment of sanatoriums in warm climates for these children with damaged lungs. Freedom from recurrent infections for a year or more would aid complete healing of existing inflammatory processes more than any other single therapeutic measure. That it is possible to secure excellent results by such a regimen is illustrated not only by the first 3 cases in table 6 but by the many patients who present themselves for treatment in the chest clinic.

It is not claimed that all cases of bronchiectasis can be eventually eliminated, for there will always occur infections that are overwhelming and there will always be pulmonary obstructions that cannot be readily removed. Fortunately these conditions are in the minority. In the majority of cases the condition is amenable to treatment and subject to control. The significance of the potential state as a precursor of bronchiectasis must be appreciated by the pediatrician, for the responsibility of preventing progressive damage rests with him. In 1909 Ewart[17] aptly phrased the task of the pediatrician in these words: "In the vital interests of our patients we must learn to suspect the presence of the affection early, so as to forestall its evolution; thus simplifying the task of treatment almost to one of prophylaxis."

17. Ewart, W.: Morbid Anatomy of Bronchiectasis, in Allbutt, T. C., and Rollston, H. D.: A System of Medicine, by Many Writers, London, Macmillan & Company, 1909, vol. 5, p. 127.

Abstracts from Current Literature

Anatomy and Physiology

Physiologic Availability of Fluids in Secondary Shock. H. A. Davis, Arch. Surg. **35**:461 (Sept.) 1937.

Recognizing that the central factor in the production of traumatic shock is the reduction of the volume of the blood, Davis experimented with the administration of various fluids to note the effect of fluid increases on the flow of blood through peripheral blood vessels. Utilizing dogs for the experiments, he noted how adequate fluids are in the treatment of shock and the criteria that can be considered most significant in the estimation of the depth of shock. The experiments showed that the introduction of fluid into the intact animal produces a dilution of the blood, with subsequent diuresis, and that additional amounts may lead to pulmonary edema. In secondary shock the normal reservoir action of the blood for fluids is lost, and fluid leaves the blood stream more rapidly than in the intact animal. A peculiar alteration of the response to fluids in traumatic shock results in a diminished availability of water even to the point of actual intolerance. Even the transfusion of blood can be harmful. An intact animal may be given fluid to the extent of 25 per cent of the total weight of the body without any diminution in the rate of consumption of oxygen, while in traumatic shock the administration of a quantity of fluid equivalent to from 5 to 12 per cent of the body weight may result in a fall in the metabolic rate.

Kaiser, Rochester, N. Y.

An Analysis of the Cardiac Irregularities Produced by Calcium, and Their Prevention by Sodium Amytal. H. E. Hoff and L. H. Nahum, J. Pharmacol. & Exper. Therap. **60**:425 (Aug.) 1937.

Administration of calcium salts by vein is occasionally followed by cardiac irregularities and rarely by death from cardiac failure. Hoff and Nahum found that the use of sodium amytal for obtaining narcosis obviated such irregularities and failure in rabbits.

Pilcher, Cleveland.

Relative Effectiveness of Atropine and Novatropin on the Gastric and Colonic Motility of the Unanesthetized Dog. J. P. Quigley, J. Pharmacol. & Exper. Therap. **61**:30 (Sept.) 1937.

Quigley has had considerable experience in this type of work. His experiments showed that the two drugs act similarly on the stomach and colon, except that atropine is somewhat more inhibitory on the stomach and considerably more so on the colon. The action of atropine is more prolonged.

Pilcher, Cleveland.

Biochemistry; Bacteriology, and Pathology

A Differential Medium for the Meningococcus and Gonococcus. S. F. Bailey, J. Bact. **34**:645 (Dec.) 1937.

The meningococcus and the gonococcus often give rise to lesions in the human being which are of the gravest import. It is therefore highly desirable that a differential diagnosis between these two and other gram-negative cocci should be made as early as possible. Workers in hospital laboratories have encountered various difficulties in the practical differentiation of these organisms. The diffi-

culties lie mainly in the slowness of acid production on solid mediums in general use and in the frequent failure of the organisms to multiply in fluid mediums. Numerous attempts have already been made to remedy these difficulties.

Bailey has prepared a medium which offers a practical means of making an early differential diagnosis. The medium consists of whole serum from which the fermentable substances and diastase have been removed and to which have been added a concentrated broth containing inorganic salts and an indicator. Differential identification can usually be established in from twelve to twenty-four hours. In contradistinction to all other bacteria studied, including several members of the streptococcic, staphylococcic, diphtheric and colon-typhoid groups, the meningococci and gonococci, in sealed cultures, produced no change on the coagulated blood serum which had been depleted of fermentable substances and to which had been added an indicator but no carbohydrate. These two organisms can utilize only such simple protein substances as are directly available for assimilation.

STOESSER, Minneapolis.

BACTERICIDAL EFFECT OF SULFANILAMIDE ON THE GONOCOCCUS IN VITRO. H. F. WENGATZ, R. A. BOAK and C. M. CARPENTER, J. Bact. **35**:36 (Jan.) 1938.

In view of the fact that evidence is accumulating that sulfanilamide is a useful therapeutic agent for the treatment of gonococcal infection, the authors decided to investigate the bactericidal effect of sulfanilamide on gonococci in vitro. Their technic is as follows: The drug is added to Douglas' broth cultures, both with and without blood, to yield a final concentration of 0.01 per cent. This percentage of sulfanilamide is employed because reports indicate that 10 mg. per hundred cubic centimeters of blood in vivo is adequate for successful therapy. Subcultures are made at varying intervals during a one hundred hour exposure to the drug at 36 C. Ten recently isolated strains of Neisserian gonorrhoeae have been studied in this manner. With each strain a marked decrease in the number of variable organisms has been observed after an exposure of twenty hours. Failure to obtain growth in subcultures, however, was not noted until the gonococci had been subjected to the action of the chemical for at least fifty hours. The thermal death time of the gonococcus at 41.5 C. was shortened by about 50 per cent when the blood broth cultures in which the organisms were subjected to the fever temperature contained sulfanilamide in the aforementioned concentration.

STOESSER, Minneapolis.

NEW CONCEPTS OF FILTERABLE VIRUSES. W. STONE, South African M. J. **12**:45 (Jan. 22) 1938.

Stone reviews the recent literature on proteins having the properties of virus which have been isolated from various plant virus diseases and points out that such discoveries bring science close to the transition point between living and nonliving matter.

GONCE, Madison, Wis.

MONILIASIS. P. A. DON, South African M. J. **12**:49 (Jan. 22) 1938.

Don briefly describes the laboratory methods of differentiating between pathogenic and nonpathogenic monilias and remarks on the difficulties thereof.

GONCE, Madison, Wis.

Metabolism; Infant Feeding; Milk and Other Foods

VALUE OF IRRADIATED MILK IN INFANT FEEDING. WILLIAM H. CLARK, Arch. Pediat. **55**:178 (March) 1938.

Forty-one infants varying in age from 1 to 18 months were examined roentgenographically for rickets. Thirty-two suffered from variable degrees of rickets. After four months of a diet consisting of irradiated milk, 81 per cent of them were definitely helped.

ORR, Buffalo.

A Comparative Study of the Growth-Promoting and Bone-Calcifying Effects of Several Carbohydrates. J. Outhouse and others, J. Nutrition **14**:579 (Dec.) 1937.

Young male rats of the same litter were placed on diets in which from 23 to 26 per cent of the caloric intake was supplied by either lactose, sucrose or galactose. The mineral intake was controlled. Greater gains were noted among the rats on the lactose-supplemented diet but only among those allowed to feed ad libitum and only when the total caloric intake was greater than that of the rats showing no gain in weight.

Lactose was the only carbohydrate which caused acceleration in the calcification of bones, but in comparison with cod liver oil this sugar, at the levels fed, did not induce as satisfactory calcification of bones. Munns, Winnetka, Ill.

Nutritional Well-Being and Length of Life as Influenced by Different Enrichments of an Already Adequate Diet. H. C. Sherman and H. L. Campbell, J. Nutrition **14**:609 (Dec.) 1937.

The authors have previously demonstrated that diet A is adequate; that is, it supports normal growth, health, reproduction and length of life, generation after generation.

Diet B on which the rats in this experiment were fed was the same as diet A except that it contained a larger proportion of milk. This means an enrichment in calcium, vitamin A and riboflavin (called in previous papers vitamin G).

The results of the experiment indicate that the enrichment of the diet with these three factors resulted in improvement in the direction of nutritional well-being, health and longevity. Munns, Winnetka, Ill.

Effects of Small Amounts of Ethyl Alcohol on the Respiratory Metabolism of Human Subjects During Rest and Work. R. C. Grubbs and F. A. Hitchcock, J. Nutrition **15**:229 (March) 1938.

One group of investigators have concluded that the energy of alcohol is available for the performance of muscular work. More recent work indicates that muscular exercise has no effect on the rate of oxidation of ethyl alcohol, while still later work by Mitchell indicates that the energy of ethyl alcohol is to a large extent available for physiologic purposes.

Grubbs and Hitchcock have investigated the effects of small amounts of ethyl alcohol on the respiratory exchanges during rest and work. Five persons served as subjects for the experiment. The authors conclude: 1. Alcohol exerted no specific dynamic action during the first two hours after its ingestion. 2. There was no significant change in the ventilation equivalent or in the alveolar carbon dioxide following the ingestion of alcohol. 3. Utilization of alcohol while the subject was resting was greater when the alcohol was given with dextrose than when it was given alone. 4. The rate of oxidation of alcohol in the body was higher with the subject in the sitting position than when he was reclining and still higher when he was working on the bicycle ergometer than when he was sitting at rest. The results are interpreted as presumptive evidence that the muscles are capable of using the energy of ethyl alcohol in the performing of work.

Munns, Winnetka, Ill.

Drugs Transmitted Through Breast Milk: I. Laxatives. R. M. Tyson, E. A. Shrader and H. H. Perlman, J. Pediat. **11**:824 (Dec.) 1937.

Two series of investigations were carried out to determine the transmission of certain cathartics through breast milk. The cathartics used were: aloin, phenolphthalein, cascara, mild mercurous chloride, senna and rhubarb. The first

series of investigations was a clinical study to determine the effect on the mother and child of the cathartic administered to the mother. The second series of investigations was a chemical analysis of the breast milk after the administration of the drug to determine the presence of the latter in the milk.

No trace of phenolphthalein, calomel, senna or rhubarb appeared in the breast milk. Aloin was transmitted, but in 87.5 per cent of the cases in which this occurred there was no clinical evidence that the drug affected the child. Cascara gave both chemical and clinical evidence of transmission. With aloin, phenolphthalein and calomel, the clinical evidence in the chemical control series is in accordance with that found in the preliminary series. Rhubarb gave no clinical evidence of its presence in the breast milk.

RAUH, Cincinnati.

WATER METABOLISM AND SOME OF ITS APPLICATIONS IN THE PRACTICE OF PEDIATRICS. A. MUGGIA, Méd. inf. **8**:387 (Dec.) 1937.

This paper was presented at the symposium on mineral and water metabolism in children at the Fourth International Pediatric Congress in Rome in September 1937.

Water metabolism is a valuable guide when use is being made of thyroid or pituitary preparations in the treatment of certain hepatic and renal infections and endocrine disorders. To demonstrate the relation of water metabolism to the endocrine glands Muggia reviews the histories of two sisters with familial pituitary hypoplasia. The output of urine in each child was from 100 to 400 cc. a day; the metabolism was —37 per cent; the body temperature was 36.5 C. (97.7 F.); the blood pressure was 90 mm.; undernutrition, asthenia and anorexia were present. One of the children responded very well to injections of pituitary extract; the urinary output increased to 950 cc.; the basal metabolism became —18 per cent; the body temperature rose to 37.3 C. (99.1 F.); there was a gain in weight along with distinct clinical improvement. The second child did not respond so satisfactorily: The temperature and blood pressure remained low; the urinary output continued to be scanty; the basal metabolism, however, rose to —18 per cent. In spite of the laboratory evidence of improvement, the child continued to do poorly, and just before death she showed signs of dehydration and a pigmentation of the skin similar to that seen in Addison's disease.

HIGGINS, Boston.

Vitamins; Avitaminoses

METABOLISM AND MODE OF ACTION OF VITAMIN D: IV. IMPORTANCE OF BILE IN THE ABSORPTION AND EXCRETION OF VITAMIN D; V. INTESTINAL EXCRETION OF VITAMIN D. W. HEYMANN, J. Biol. Chem. **122**:249 (Dec.) 1937.

Dogs were fed a rachitogenic diet and kept in a dark room. Then ligation and transection of the common bile duct were performed, and a biliary fistula was established. Vitamin D was administered in the form of viosterol in oil or of purified vitamin D in propylene glycol (drisdol), in a dose of from 20 to 25 cc., by stomach tube or by intramuscular injection. The antirachitic efficacy of the serum of control dogs on injection into rats was found to increase considerably following oral administration of vitamin D, and hyperphosphatemia resulted. In the blood serum of the experimental dogs, no vitamin D could be detected, and hyperphosphatemia was not present. The conclusion is that bile is necessary for the absorption of vitamin D. Excretion of vitamin D into the bile occurred in the animals receiving crystalline vitamin D in propylene glycol but was negligible in those receiving viosterol in oil; the solvent seemed to determine excretion.

In dogs treated as described, vitamin D administered by mouth in the form of viosterol in oil or of purified vitamin D in propylene glycol was present in the feces for from ten to sixteen days. In control animals, vitamin D was demonstrable

for from six to eight months. After the first two weeks, vitamin D in the feces originates from a slow excretion of quantities that have first been absorbed. Vitamin D was found to be excreted in rather large amounts through the wall of the upper third of the small intestines.

LIMPER, Louisville, Ky.

ANTIRACHITIC VALUE OF IRRADIATED EVAPORATED MILK IN INFANTS: AN OUT-PATIENT STUDY. M. RAPOPORT, E. KRICK and J. STOKES JR., Pediat. **11**:782 (Dec.) 1937.

The authors have previously shown that irradiated evaporated milk is an adequate agent for the prevention of rickets in both white and Negro infants under controlled conditions in hospital wards. The present study was made to determine the antirachitic value of the same milk under ordinary conditions of practice in the clinic or home. The subjects were 108 infants who were weaned at an early age (the majority under 3½ months and none over 5 months). The period of study included the months from December to May. The milk used was assayed at intervals in random samples and found to contain from 125 to 135 U. S. P. units of vitamin D in each 14½ ounce (427.5 cc.) can. Of 97 nonrachitic infants fed this milk, 82 (84.5 per cent) were completely free from rickets, 14 acquired mild rickets, which disappeared during the period of observation, and 1 acquired mild rickets, which did not disappear. Fifty of these infants were Negroes, and 47 were white. Only 3 of the 15 infants in whom rickets developed were Negroes. Eleven infants were suffering from mild rickets in the beginning of the study. The average time for complete healing of the group was eleven weeks, the shortest time being three and one-half weeks and the longest fifteen weeks. Healing began on the average at six weeks. The authors conclude that this milk is an effective prophylactic antirachitic agent under the ordinary conditions of outpatient practice but that it is an inefficient healing agent because of the long period of time required for complete healing.

RAUH, Cincinnati.

INADEQUACY OF SYNTHETIC ASCORBIC ACID AS AN ANTISCORBUTIC AGENT. A. ELMBY and E. WARBURG, Lancet **2**:1363 (Dec. 11) 1937.

This study comes from the University Clinic of Rigshospitalet and from the University Institute for Hygiene, both in Copenhagen.

The ascorbic acid of the serum was estimated by (*a*) the macromethod of Lund and Lieck and (*b*) the micromethod of Elmby and With. The ascorbic acid in urine was estimated by the Lund-Lieck method.

A total of 29 patients were found to present signs of a hemorrhagic diathesis together with a low concentration of ascorbic acid in the serum. Each of them was given 300 mg. of ascorbic acid daily by mouth for ten days. In all but 3 this led to disappearance of the tendency toward hemorrhage and a return of the level of the ascorbic acid of the serum to normal. Each of the 3 refractory patients had received by mouth a total of 3 Gm. of ascorbic acid. Each was then given an additional 300 mg. intravenously every day for ten days, with no apparent effect. Finally each was given the juice of 10 lemons every day for ten days (each lemon was found to contain from 20 to 40 mg. of ascorbic acid). The hemorrhagic condition disappeared and the ascorbic acid of the serum returned to a normal level.

The explanation suggested is that for the absorption and retention of ascorbic acid some unknown substance (a "co-vitamin") is required. This substance is present in lemons.

The hypothesis that this factor is the same as the vitamin P found by Szent-Györgyi is being investigated.

LANGMANN, New York.

TREATMENT OF RACHITIC MYOPATHY WITH AMINOACETIC ACID. G. LODI, Méd. inf. **8**:381 (Dec.) 1937.

Hypotonia and weakness of muscles are characteristic findings in rickets. Even after the bone changes are remedied by vitamin D or by ultraviolet radia-

tion, the muscular weakness may persist. Lodi reports a case of active rickets in a child of 2 years; she was given 8 Gm. of aminoacetic acid daily for three periods of three weeks each. Photographs of the child at the end of each period portray the satisfactory return of muscular tone and strength.

HIGGINS, Boston.

THE VITAMIN C CONTENT OF THE BLOOD PLASMA IN NORMAL AND SICK CHILDREN. F. T. CHU and C. SUNG, Chinese M. J. **52**:791 (Dec.) 1937.

From the division of pediatrics of the Peiping Union Medical College, these authors report the vitamin C content of the plasma and the urinary response to repeated daily test doses of the vitamin. The content of the plasma was higher in breast fed than in artificially fed infants. An amount of fruit juice which was sufficient to raise the vitamin C content of the plasma in normal infants did not change the low level of this vitamin in the blood plasma of infants with diarrheal or dysenteric stools. The number of cases was adequate for making the experiments conclusive.

Infants with kala-azar seemed to have a lower level of vitamin C in the plasma when the condition was complicated by noma. The lower level was found also in children suffering from typhoid fever and tuberculosis.

NEFF, Kansas City, Mo.

EXPERIMENTAL DETERMINATIONS OF THE INDISPENSABLE REQUIREMENTS OF VITAMIN C (ASCORBIC ACID) OF THE PHYSICALLY HEALTHY ADULT. G. F. GÖTHLIN, E. FRISELL and N. RUNDQVIST, Acta med. Scandinav. **92**:1, 1937.

Four schizophrenic but physically healthy adults between the ages of 23 and 43 at the Ulleraker Mental Hospital were selected to be fed a "basal diet" containing only 2 mg. of ascorbic acid per day which was combined with a supply of chemically pure ascorbic acid according to a certain plan. The period of the investigation, which varied between six and eight months for the different subjects, was divided into three week stages. During each stage the daily addition of ascorbic acid was constant. During the first stage it was 1 mg. per person. Then it was successively increased from stage to stage. At the end of each three week stage, both arms of the test persons were subjected to a first treatment with 35 mm. overpressure, according to Göthlin's method, and subsequently a count of petechiae was made. On the following day the corresponding procedure with 50 mm. overpressure was carried out, and the fresh petechiae were counted.

With the smallest doses of ascorbic acid, the petechial index increased from stage to stage. With 0.15 mg. of ascorbic acid per kilogram of body weight, a change took place. The petechial index began to fall, and with further increase in doses it approached closer and closer to the normal value met with at the beginning of the investigation. Normal conditions in the strength of the cutaneous capillaries and full protection against the capillary fragility which follows a deficiency of ascorbic acid were attained in the 4 test persons with a daily supply of ascorbic acid in amounts between 0.35 and 0.45 mg. per kilogram of body weight.

The authors state that it is out of the question that the flavones described by Rusznyák, Szent-Györgi and others as permeability vitamins, the supply of which they found caused the petechiae in vascular purpura to disappear temporarily, could have played any part in the disappearance of the petechiae in their investigation since the only alteration from period to period in this dietary experiment was a change in the daily ration of chemically pure ascorbic acid.

FROM AUTHORS' SUMMARY.

WHEN IS CAPILLARY FRAGILITY A SIGN OF A SUBNORMAL SUPPLY OF VITAMIN C IN MAN? G. F. GÖTHLIN, Acta pædiat. **20**:71, 1937.

In 1930 Göthlin showed that a diet which is extremely poor in vitamin C gradually gives rise to increased capillary fragility. Göthlin's work has been confirmed by other investigators and has been supplemented by subsequent observations of his own. The most important of the conclusions which were drawn from the earlier studies is that the indispensable requirement of vitamin C for man is that supplied by the oral ingestion of from 0.7 to 1 cc. per kilogram of body weight daily of the juice of fresh yellow Mediterranean oranges. In terms of ascorbic acid this is equivalent to between 0.39 and 0.48 mg. per kilogram per day. The capillary fragility test also made it possible to demonstrate seasonal fluctuations in the vitamin C content of the diet of the inhabitants of Sweden, both adult and child.

Despite the identification of vitamin C and the development of direct chemical methods for its estimation, the capillary fragility test retains clinical usefulness inasmuch as it can be carried out with simple equipment and does not require venipuncture. In order that the results of the test may be reliable and comparable with those of other investigators, the technic must conform closely to Göthlin's highly explicit directions. Conclusions relating to a person's supply of vitamin C can be drawn from a single test only when that person is in good health; i. e., when he is not suffering from diseases which have the effect of lowering the resistance of the capillaries to overpressure. In dealing with sick patients and in cases where a single test yields equivocal results, it is frequently possible to arrive at definite conclusions by administering large quantities of ascorbic acid and repeating the test after an interval of a week or ten days. The test becomes positive when the concentration of ascorbic acid is approximately 1 mg. per liter of blood. However, the correlation between the number of petechiae which appear under standard conditions and the concentration of ascorbic acid in the blood is not sufficiently exact to permit quantitative prediction of the latter from the former.

The author's claims for the usefulness of his method are modest and precise; they appear to be well substantiated. The bibliography is serviceable.

McCUNE, New York.

SCURVY AND DIABETES. B. SÖDERLING and B. HAMNE, Svenska läk.-tidning. **34**:1600 (Nov. 19) 1937.

A 10 year old diabetic girl, treated for two and one-half years with insulin and a nonrestricted diet ("free diet"), had during the last year displayed poor tolerance for carbohydrates combined with diminished sensitivity to insulin. At a control examination in August she was found to be suffering from manifest scurvy, and her carbohydrate metabolism was unsatisfactory, with acidosis and wasting. It was probable that she had had latent scurvy for at least eight months previously. After administration of large doses of ascorbic acid there was rapid improvement. Parallel with the disappearance of the clinical signs of C avitaminosis she acquired a much better tolerance of carbohydrate and responded well to the treatment with insulin. The authors believe that some of the so-called insulin resistance of patients with diabetes and the seasonal deterioration of the metabolism of carbohydrate may be due to an insufficient supply of vitamin C. They are of the opinion that diabetic patients have a greater need of this vitamin because of the supposed antagonistic effect of the foodstuffs containing vitamin A (principally fat and egg) in the diabetic person's diet.

WALLGREN, Göteborg, Sweden.

PREVENTIVE TREATMENT OF RICKETS WITH COD LIVER OIL. A. MADSEN, Ugesk. f. læger **99**:1286 (Dec. 2) 1937.

During the winter months 147 infants received a supply of vitamin D corresponding to from 200 to 400 international units per day. Of these infants from

2 to 3 per cent showed very slight rachitic signs roentgenologically, while 50 per cent of 70 infants who had no extra supply of vitamin D acquired rickets.

WALLGREN, Göteborg, Sweden.

AN INVOLUNTARY PROOF OF AVITAMINOSIS AS A CAUSE OF RICKETS. E. J. MEYERS, Nederl. tijdschr. v. geneesk. **81**:5534 (Nov. 13) 1937.

An infant 15 months old acquired severe rickets as a result of being fed a diet free from vitamin D in consequence of a strict following of the prescriptions of a natural healing method.

VAN CREVELD, Amsterdam, Netherlands.

Hygiene; Growth and Nutrition; Public Health

A RAPID AND ECONOMICAL METHOD OF "DELOUSING." C. LEBAILLY, Rev. méd.-sociale de l'enf. **5**:335 (Sept.-Oct.) 1937.

Brief mention is made of a simple cabinet in which patients and their clothing may be placed. Of particular interest, however, is the apparatus for eradicating head lice. This apparatus is an impervious hood which fits tightly around the neck and leaves the face exposed. A portable generator of sulfur dioxide is used to inflate the hood. The patients are kept outdoors for the duration of the twenty minute treatment. A second treatment is given seven or eight days later, and usually no more are necessary. The treatment is recommended because of its economy, simplicity (if one has the equipment) and efficacy.

DIETRICH, Beverly Hills, Calif.

HISTORY, MORALS AND PEACE THROUGH THE SCHOOL. F. J. PICAREL, Bol. Inst. internac. am. de protec. a la infancia **11**:289 (Jan.) 1938.

Picarel's opinion is that history taught with a moral aim should awaken in pupils an earnest civic enthusiasm and the reverence due to men whose deeds have been illustrious according to the consecrating judgment of posterity. History so taught should on one hand exemplify patriotism, self denial and human solidarity and should on the other produce a healthy optimism as to the value of effort in the service of a worthy and honorable cause. Further on he stresses the fact that the teaching of history as just explained may have a fundamental influence in the formation of a peace-making conscience.

FROM AUTHOR'S SUMMARY.

MEASURES PREVENTIVE AGAINST MORTALITY OF INFANTS DUE TO FEEDING DISTURBANCES. R. BERRO and J. A. BAUZÁ, Bol. Inst. internac. am. de protec. a la infancia **11**:397 (Jan.) 1938.

Speaking of Uruguay, Berro and Bauzá state that diseases of the digestive system are the chief causes of death among infants. Breast feeding is most common during the first three months of life; the next three month period, when cow's milk or other foods are added to the diet, is a dangerous time for the child. In summer, climate is a decisive factor in infant mortality, the death rate depending on the intensity of the heat.

The control of all dependent infants by the state during their first two years of life is a provision of the Children's Code which is already carried out in Montevideo. The health supervision of such children promotes breast feeding, and this teaching is promoted at the child health centers, in the rooms where mothers suckle their babies in factories, in the lunch rooms for nursing mothers and at other points.

An experience of thirty years has established the advantage of dry milk in the prevention of feeding disturbances when mothers cannot be provided with fresh cow's milk and a refrigerator or other means of preserving milk.

Economic aid to poor mothers is fundamental. At the Casa del Nino, $19,805.95 was spent in 1936 to meet 1,099 demands, which means an average expense of $18 for every demand. Although this is a small sum, it was sufficient to prevent 130 mothers from abandoning their children. Among the mothers served, 648 were unmarried, 41 widowed and 98 abandoned by their husbands. The money that was not given in cash was spent in the form of feeding certificates, first aid allowances and house rent. The authors suggest that in order to get the necessary funds Italy's example of taxing unmarried persons might be imitated.

The government has made provisions for establishing three crèches and day homes and two mother and child centers, also for building several groups of workmen's houses.

FROM AUTHORS' SUMMARY.

MEDICOSOCIAL CARE OF INFANTS. R. BERRO, Bol. Inst. internac. am. de protec. a la infancia **11**:408 (Jan.) 1938.

Berro, who is the president of the Child's Council of Uruguay, studied the medicosocial work done by this agency in behalf of infants and then lectured on the subject before the Society of Pediatrics in Rio de Janeiro, Argentina.

He believes that the time has arrived for American countries not to expect an increase of their population through immigration: They should seek to increase the birth rate and to decrease infant mortality by an intense child-caring campaign.

The problem is unitarian: the mother and child are inseparable before, during and after the birth of the child. It is especially fundamental to prevent the separation of the child from its mother. Such a separation not only increases the risk of diseases for the child, who in that case is more liable to be sick than healthy, but breaks the social unity of the organized family.

The Casa del Nino in Montevideo, Uruguay, is a real mother and child center, an infant health center.

FROM AUTHOR'S SUMMARY.

FIRST CONGRESS OF SCHOOL HYGIENE IN LA PLATA, ARGENTINE REPUBLIC, 1937. L. M. PETRILLO, Bol. Inst. internac. am. de protec. a la infancia **11**:425 (Jan.) 1938.

Twenty-eight recommendations are made in relation to school hygiene.

LESLIE, Evanston, Ill.

STATIONS FOR COLLECTING BREAST MILK. M. E. KAYSER and H. MOMMSEN, Med. Klin. **33**:45 (Jan. 14) 1938.

The discussion under this title consists of two articles. In the first Kayser takes issue with Mommsen, who in an article in a previous number (*Med. Klin.* **33**:1558 [Nov. 19] 1937) contended that boiling renders breast milk the worst food for artificially fed infants with nutritional disturbances. Kayser relates her own experience and quotes Thiemich and Birk to the effect that boiling has no deleterious influence on breast milk. She hints that adulteration and faulty preservation may lead to erroneous conclusions regarding the value of breast milk.

In the second article Mommsen reiterates that breast milk is the ideal food for the infant when taken directly from the mother's breast and concedes that it is indispensable for premature infants. However, he insists that breast milk (raw or boiled) is bad for artificially fed infants with severe nutritional disturbances and quotes other authors in support of his contention.

SIEMSEN, Chicago.

PHYSICAL TRAITS OF PEIPING CHILDREN: STATURE AND WEIGHT MEASUREMENT FROM ONE MONTH TO THREE YEARS OF AGE. R. A. GUY, C. C. CHIANG, H. H. HUANG and K. S. YEH, Chinese M. J. **52**:507 (Oct.) 1937.

The authors, under the Department of Public Health, Peiping Union Medical College and the First Health Station of Peiping, collected measurements of

healthy children who had been nursed at the breast. Children of every economic status were included. The methods are given in detail and the results in tabulated form. The weights and lengths of male infants are identical with those of Iowa infants for the first four months of life but are somewhat less than those measurements after that age period. Infants of the age of 9 or 10 months, below 70 cm. in length, are relatively heavier than Vienna infants. The authors cannot state that these characteristics are due to race rather than to food. The figures are to be used in the assembly of data on the Chinese people, so that their racial or geographic traits may be compared with those of other races.

NEFF, Kansas City, Mo.

MEASURING INFANTS AND CHILDREN: CHOICE OF MEASUREMENTS, EQUIPMENT AND TECHNIQUE. P. H. LI, F. T. CHU and P. H. STEVENSON, Chinese M. J. **52**:549 (Oct.) 1937.

These physicians in the Peiping University Medical College, division of pediatrics and department of anatomy, publish illustrations of apparatus developed for the accurate measuring of total height, vertex-symphysis distance, symphysis to sole distance, sitting height, shoulder breadth, cristal breadth, circumference of the head and of chest and the span of arms. Children under 6 years are weighed without clothing and older ones with one piece of underclothing. The weights are taken in grams. The significance of each type of measurement is discussed.

NEFF, Kansas City, Mo.

Prematurity and Congenital Deformities

ECTOPIA CORDIS CUM STERNI FISSURA: A CASE STUDY. R. N. BARLOW, J. Pediat. **12**:58 (Jan.) 1938.

A case of displacement of the heart with sternal fissure not covered by skin or parietal pericardium is described. The baby lived for sixty hours, and during this time electrocardiographic studies were made. The conductivity within the heart was found to be normal. The conductivity through the body was found to be impaired so much that no deflections were obtained with the conventional leads from the extremities, thereby tending to disprove the theory of blood vessel conductivity.

RAUH, Cincinnati.

THE DEVELOPMENT OF THE "RIGHTING" MOVEMENTS IN THE FOETAL SHEEP. J. BARCROFT and D. H. BARRON, J. Physiol. **89**:19P, 1937.

Between the forty-seventh and the fiftieth day of intrauterine life (the total gestation period being about one hundred and fifty days), the fetal sheep, when lying on a solid surface, attempts to raise its head and to stand (with the forelimbs extended and the hindlimbs flexed at the hip) in response to stimulation of the snout. This response is not obtainable at either earlier or later periods of fetal life.

MCCOUCH, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

CRANIOFACIAL DYSOSTOSIS (CROUZON'S SYNDROME). R. W. B. ELLIS, Proc. Roy. Soc. Med. **30**:1187 (Aug.) 1937.

Ellis reports a case of craniofacial dysostosis in a boy of 12 years, who was admitted to the hospital on account of unresolved pneumonia. On physical examination this boy was found to have oxycephaly and bilateral flattening of the frontal region. The eyes were widely separated and showed bilateral external strabismus. Each iris showed a congenital coloboma. The sight was grossly defective. The upper lip was short and the palate high and arched.

The characteristic features of Crouzon's syndrome are hypertelorism, the association of oxycephaly with exophthalmos, optic atrophy and a high arched palate. Coloboma of the iris is also not an infrequent associated finding. Prognathism was not so marked in this case as usual.

The report is accompanied by pictures of the boy.

WILLIAMSON, New Orleans.

A CASE OF ACROCEPHALOSYNDACTYLISM. W. S. RIBEIRO, Arch. de pediat., Rio de Janeiro **10**:173 (Jan.) 1938.

The boy was 3 years of age, the first born, and there was no family history of such an anomaly. Roentgenograms of the skull and photographs of the extremities and the retina are shown.

SANFORD, Chicago.

ESTENOCEPHALIA. A. AUGUSTO, Arch. de pediat., Rio de Janeiro **10**:293 (March) 1938.

Included in this term are scaphocephaly, acrocephaly, platycephaly and trigonocephaly. Photographs and roentgenograms to illustrate these conditions are shown.

SANFORD, Chicago.

CONGENITAL HERNIA OF THE DIAPHRAGM. O. HELLER and A. LÖW-BEER, Kinderärztl. Praxis **8**:461 (Nov.) 1937.

This is a description and discussion of a case in a boy 7 years of age. For years he had suffered from recurrent abdominal pains in the region of the umbilicus. He was admitted to the hospital because of ileus. Roentgenographic examination revealed dextrocardia, the heart having been displaced by an intestinal loop in the left side of the thorax. The authors conclude that every case of recurrent umbilical colic or of ileus warrants roentgenographic examination because of the possibility of diaphragmatic hernia.

HEYMANN, Cleveland.

NURSING AND THERAPEUTIC CARE OF APNEA AND ASPHYXIA IN PREMATURE INFANTS. HOFFMANN, Kinderärztl. Praxis **8**:510 (Dec.) 1937.

Trauma of the brain and hemorrhage into the brain do not play an important role in the etiology of apnea and asphyxia in the premature infant. One should therefore be more active in the treatment of premature infants for these conditions, which the author believes are due mainly to immaturity and underdevelopment of the breathing center. Formulas should be given frequently, in very small amounts. The utmost care should be taken in regulating the temperature of the infants. Administration of oxygen is not considered of decisive influence. Use of lobeline in combination with metrazol or a 25 per cent solution of pyridine betacarbonic acid diethylamide (coramine) and, if necessary, with daily subcutaneous infusions of 5 per cent dextrose in Ringer's solution, is highly recommended.

HEYMANN, Cleveland.

NUTRITIONAL REQUIREMENT OF PREMATURE INFANTS. J. TANZ and H. UNGER, Ztschr. f. Kinderh. **5**:135 (Oct. 14) 1937.

Some authors consider the caloric requirement of premature infants to be high and advocate an intake high in calories. Others recommend minimal feeding during the early part of the premature infant's life because of the tendency toward nutritional upsets through overstepping tolerance. The authors report their experience with minimal nutrition during the first few weeks and regard such nutrition as advisable. Graphs and tables accompany the report.

SIEMSEN, Chicago.

RARE FETAL MONSTERS WITH REPORT OF TWO CASES. S. W. LEE, Chinese M. J. **52**:879 (Dec.) 1937.

Two monsters of rare type, one a syncephalus and the other a cyclocephalus, are reported from the Central Hospital of Nanking. The former consisted of three upper and three lower extremities, all well formed, and two other decidual limbs, preventing extraction without dissociation. The latter monster had one eye and no mouth.

NEFF, Kansas City, Mo.

Newborn

VALUE OF A COD-LIVER OIL CONCENTRATE IN PREVENTING WEIGHT LOSS IN THE NEW-BORN. J. R. DOLCE, Arch. Pediat. **55**:185 (March) 1937.

A reduction in the loss of weight in 18 of 22 newly born infants is attributed to the use of cod liver oil concentrate in the diet. Similar reductions were reported in 17 infants who were being anointed with an antiseptic oil enriched with vitamins A and D.

ORR, Buffalo.

EPIDEMIC DIARRHEA OF THE NEWBORN: II. CONTROL AND PREVENTION OF OUTBREAKS IN HOSPITAL NURSERIES. S. FRANT and H. ABRAMSON, J. Pediat. **11**: 772 (Dec.) 1937.

During the past few years outbreaks of highly fatal diarrhea of unknown cause have been occurring among newborn babies in hospital nurseries of New York City and elsewhere. Among 3,672 liveborn babies exposed to the disease during sixteen outbreaks in the period from July 1934 to December 1936, 505 acquired this diarrhea, a morbidity rate of 14 per cent. Of the babies stricken, 234 are known to have died. The mortality rate was 6 per cent when based on the number of infants exposed and 46 per cent when based on the number of those stricken.

In order to control epidemics of this disease the Sanitary Code of New York City was amended to include as a reportable condition all "Diarrhea in the newborn up to 3 weeks of age occurring in a hospital giving maternity service." A careful check is made of all death certificates of infants dying under 1 month of age throughout the city. Each death is traced to the institution of birth regardless of the given cause of death and the accuracy of the diagnosis. Immediate closure of maternity wards and nurseries for newborn is ordered as soon as any cases are reported, and services are suspended until it is certain that no new cases will develop among babies who have been in contact with the disease and until the nurseries and pediatric wards have been cleared of all sick newborn infants. Those with the primary and those with secondary cases of the disease are isolated. All newborn babies that have been in contact with the disease are observed for a minimal period of three weeks before being discharged as normal. The adoption of a technic of "aseptic nursing" is insisted on, as well as complete segregation of the maternity floor from the rest of the hospital. The entire physical equipment of the maternity service is inspected for sanitary defects. Cultures are taken from every source of contamination and from all materials coming in contact with the babies. Cultures are made of nasal and pharyngeal secretions and of stools of all infants, their mothers and the entire personnel. Carriers of any known infectious organisms are excluded from the maternity division. The authors feel that there is evident a lack of precautions which would aid in the prevention of the diarrheal disorder. They feel that efficient and workable measures can be taken which would prevent these epidemics, and they outline in detail a technic of "aseptic nursing" to be carried out in all maternity nurseries to include not only the newborn infants but the mothers and all maternity personnel as well.

RAUH, Cincinnati.

A Study of Large-Sized Newborn Infants. R. S. Cuizza, Lattante **8**:655 (Dec.) 1937.

Of 8,892 infants, 471, or 5.1 per cent, weighed more than 4,000 Gm. at birth. Of these large-sized infants, 64 per cent were boys. They were generally not the first-born infants. Their lengths and the circumferences of their heads and chests were also increased. The physiologic loss of weight during the first few days of life was greater than in the infants of normal weight, and the rate of growth was slower. Dentition was earlier. The large infants were much more subject to the dangers of childbirth, especially asphyxiation, but aside from this they showed no pathologic tendencies except an exudative diathesis. In general, aside from the danger at birth, there was nothing to indicate that a large newborn infant has a less favorable prognosis than a newborn infant of normal weight.

Higgins, Boston.

Congenital Diaphragmatic Hernia in a Newborn Infant. G. Cardelle, R. Pereiras and F. Sala Panisello, Arch. de med. inf. **6**:388 (Oct.-Dec.) 1937.

The child presented a hernia of the left side of the diaphragm, through Bochdalek's gap. The colon and small intestine were in the thoracic cavity. The child died before operation. Therefore the authors advise immediate operation. The differential diagnosis is between pulmonary cyst, pulmonary abscess, false pneumothorax, subphrenic abscess and eventration or paralysis of the diaphragm.

Sanford, Chicago.

The Treatment of Asphyxia in the Newborn. E. Poeck, München. med. Wchnschr. **84**:330 (Feb. 26) 1937.

Poeck's thesis is that the proper treatment of asphyxia of the newborn is frequently a matter of prophylaxis. The prophylaxis consists in correctly treating intrauterine asphyxia. Signs of intrauterine asphyxia during labor necessitate rapid and often instrumental delivery. The asphyxia of the newborn infant is treated by mechanical stimulation, by clearing the air passages and by injecting cardiac or respiratory stimulants. These measures are often unsuccessful because they are administered too late. According to Poeck, a cardiac or respiratory stimulant (metrazol) should be given during labor, either to the mother (by intravenous or intramuscular injection) or directly to the fetus via the presenting part (scalp or buttocks).

Brahdy, Mt. Vernon, N. Y.

The Weights and Measurements of the Mature New-Born Child. Gordon King and T'ang Yü Teh, Chinese M. J. **52**:501 (Oct.) 1937.

This instalment of a contribution entitled "Obstetrical Criteria in North China" reports the findings in 1,000 consecutive infants delivered at Cheeloo University Hospital, Shantung, China, for the five years ending in 1936. The height of male infants averaged 49.91 cm.; that of female infants, 49.07 cm. The weight of male infants averaged 3,138 Gm. and that of female infants 3,038 Gm. Fetal measurements generally were found less than the standards in Western countries.

Neff, Kansas City, Mo.

Acute Appendicitis in a Newborn Infant. Y. H. Ch'eng and H. J. K'ang, Chinese M. J. **52**:876 (Dec.) 1937.

There had been only 2 children among the 310 persons admitted for appendicitis at the Central Hospital of Nanking, until the present instance of a newborn infant with the disease. On the third day of life the child became sick with abdominal distention which was apparently due to intestinal obstruction. The white blood

count of 11,000 on the first day of illness changed in the course of the disease to 21,000, of which 61 per cent were neutrophils. No operation was attempted, because appendicitis was not considered. Autopsy showed the presence of inflammation of the appendix with acute diffuse fibropurulent peritonitis.

NEFF, Kansas City, Mo.

Acute Contagious Diseases

AN INFECTION OF CHICK EMBRYOS WITH HAEMOPHILUS PERTUSSIS REPRODUCING THE PULMONARY LESIONS OF WHOOPING COUGH. M. GALLAVAN and E. W. GOODPASTURE, Am. J. Path. **13**:927, 1937.

Chick embryos are susceptible to infection with Haemophilus pertussis. Infection of the respiratory tract, including the lungs of the embryo, has been induced by infection of the chorioallantoic membrane and by inoculation of the amniotic fluid with H. pertussis. The pulmonary infection of the embryo reproduced the pulmonary lesions of human whooping cough in detail. These lesions were characterized by growth of H. pertussis on the ciliated border of respiratory (and other) ciliated epithelia, necrosis and inflammation of the middle and basal layers of the epithelial membrane, intrabronchial and peribronchial cellular exudation and alveolar and interstitial pneumonia. These experiments indicate that H. pertussis alone is the inciting cause of whooping cough.

FROM AUTHORS' SUMMARY. [ARCH. PATH.]

SPECIFICITY OF THE LESION OF EXPERIMENTAL MUMPS. O. BLOCH JR., Am. J. Path. **13**:939, 1937.

Focal acinar necrosis, i. e., necrosis involving all or most of the cells of an acinus, is the fundamental lesion of experimental mumps, the lymphocytic reaction, edema and hemorrhage being subsequent factors. This particular type of necrosis was produced with none of the inert or infectious substances injected, though some of them may have caused the death of a cell here and there or produced an abscess destroying large numbers of acini. Cytoplasmic inclusion bodies, though found in the glands in over half the cases of mumps, may also be found in glands which have received an injection of normal saliva and cannot therefore be regarded as a specific sign of mumps infection. The abundance and interacinar location of the lymphocytic exudate are suggestive evidence that the lesion is due to infection rather than to an inert substance but do not aid in distinguishing between different types of infection. It should be stated that in no condition other than mumps did a secondary enlargement, with edema of the gland and elevation of temperature, occur. This seems to be characteristic of mumps, as is likewise the histologic lesion.

FROM AUTHOR'S CONCLUSION. [ARCH. PATH.]

PREVENTION AND MODIFICATION OF MEASLES. C. R. MCKHANN, J. A. M. A. **109**: 2034 (Dec. 18) 1937.

The diminishing mortality, the causes and the contagiousness of measles and immunity to the disease are discussed.

Figures obtained from the literature show that placental extract, convalescent serum and adult serum rate in that order in the prevention and modification of measles. McKhann's placental extract, used in over 2,000 cases, gave modification or prevention in about 93 per cent of the cases. The incidence of reactions is discussed. The optimal procedure for modification of the disease in the exposed is to give on the eighth day a dose which when given at an earlier date is ordinarily preventive.

HEERSMA, Kalamazoo, Mich.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **52**:1875 (Dec. 24) 1937.

For the period of Nov. 7 to Dec. 4, 1937, 15,867 cases of measles were reported, which is much above the seasonal incidence. The incidence of smallpox, with 910 cases, is also higher. The incidence of influenza and that of meningitis were only slightly above the usual. The incidence of poliomyelitis, of typhoid and of scarlet fever was low, while that of diphtheria, with 3,676 reported cases, was the lowest it has been in the last nine years. The mortality from all causes in large cities was 11.2 per thousand. This is about average. SANFORD, Chicago.

PREVENTION OF DISABILITY. A SYMPOSIUM: THE EARLY DIAGNOSIS AND MEDICAL TREATMENT OF POLIOMYELITIS. H. K. TENNEY, Wisconsin M. J. **36**:900 (Nov.) 1937.

The three modes of onset of poliomyelitis are: (1) the rare mode in which no symptoms are manifested before the occurrence of paralysis; (2) the dromedary mode, in which the general preliminary symptoms subside in from one to two days and then return to be followed by paralysis. The first phase is chiefly gastrointestinal or respiratory; (3) the usual mode, in which general systemic symptoms progress steadily to involvement of nerve tissue.

The New York classification of poliomyelitis into three types is also given as follows: (1) the abortive type, with general symptoms but no neurologic involvement; (2) the nonparalytic type, in which there are only transient neurologic symptoms; (3) the type with subcortical paralysis, including the usual spinal and bulbar types; (4) the encephalitic type, including those with marked stupor; (5) the ataxic type, with cerebellar involvement.

The usual physical findings, the laboratory tests and the differential diagnosis are covered, with particular mention of the fact that true poliomyelitis may occur with a normal spinal fluid, that the sugar is reduced and that the colloidal gold curve is quite constant, with its changes in the lower dilutions.

As to treatment, drugs are believed to have little value; serums and vaccines, doubtful value. A spinal tap is a definite aid. JANNEY, Wauwatosa, Wis.

PREVENTION OF DISABILITY. A SYMPOSIUM: THE PREVENTION OF DISABILITY IN POLIOMYELITIS. H. L. GREENE, Wisconsin M. J. **36**:903 (Nov.) 1937.

Orthopedic treatment should begin simultaneously with medical care. If proper orthopedic treatment is started early, deformity need not develop. Paramount is absolute physiologic rest, acquired by carefully supervised splintage in neutral positions. This should be continued for from six to seven weeks, or until all tenderness has disappeared. One must constantly keep in mind toe drop and back knee. The mattress should be supported so that it will not sag. Early testing for muscle power is condemned. Reeducational exercises after all muscle tenderness has subsided should not produce pain or fatigue. Muscle training, given chiefly in warm water baths, should be preceded by baking and mild massage. In the absence of hydrotherapy, a method of supporting the part to be treated in an overhead sling is valuable.

In the stage of convalescence the chief objectives are: (1) to make a complete muscle chart showing the extent of the paralysis and the comparative strength of the muscles, (2) to watch for and prevent deformity, (3) to stimulate circulation and increase nutrition, (4) to promote relaxation and rest, (5) to protect muscles from overstretching, (6) to prevent contracture and (7) to reeducate and strengthen muscles by suitable exercise.

Functional use should also avoid fatigue and overstraining. Watch particularly that (1) the foot on the sound side in cases of unilateral involvement does not become flat from overwork and that (2) scoliosis and pelvic deformity do not develop because of a short leg.

Braces should be worn when walking is first allowed, which is at from six months to one year. After a year of reeducational effort and bracing, operative reconstruction may be done to prevent deformity and restore function.

JANNEY, Wauwatosa, Wis.

TREATMENT OF THE RESPIRATORY FAILURE OF POLIOMYELITIS. H. MCLORINAN and J. WATSON, M. J. Australia **2**:1123 (Dec. 25) 1937.

The authors discuss the details of the management of patients in respirators. No analysis of results is presented except to say that "in those cases of respiratory failure in which there is no bulbar involvement, respirator treatment is of the utmost value."

GONCE, Madison, Wis.

MULTIPLE PYAEMIC ABSCESSES IN SCARLET FEVER; OPERATIONS; RECOVERY. J. D. ROLLESTON and P. TURNER, Proc. Roy. Soc. Med. **31**:70 (Dec.) 1937.

A boy aged 5½ years who was suffering from scarlet fever was admitted to a hospital on May 11, 1936. On May 15 otorrhea developed on the left side; on May 19, osteomyelitis of the left ulna; on May 27 suppurative arthritis of both ankles and of the right elbow joint; on June 1, suppuration of the right knee joint; on June 23, a subcutaneous abscess over the sacrum and on July 9, an abscess of the right thigh. By August 12 all wounds were healed, and he was allowed to be up, but he could not walk by himself until September 15, and it was not until the summer of 1937 that he recovered complete movement of all his joints.

WILLIAMSON, New Orleans.

SEROTHERAPY IN THE TREATMENT OF DIPHTHERITIC PARALYSES. R. CRUCHET and E. GINESTOUS, Arch. de méd. d. enf. **40**:725 (Nov.) 1937.

A discussion which began thirty years ago, concerning the efficacy of serum therapy in paralysis following diphtheria, has been reopened. At the Children's Hospital of Bordeaux, France, between 10 and 15 cases of such paralysis are observed annually, and the authors' experience with specific treatment has been most satisfactory.

The work of Ferré in 1897 and the years following showed that in diphtheria of fowls injection of the avian toxin was followed by paralysis of the diphtheritic type; it also proved that such results could be wholly prevented or greatly minimized by subsequent injections of antitoxin.

In opposition to this theory, many clinicians assert that specific serum is ineffective in both associated and isolated paralysis and that when recovery occurs it is spontaneous.

Cruchet and Ginestous report cases in defense of the doctrine of specific therapy and offer the following conclusions:

1. The dosage of serum on the first day should be from 40 to 60 cc., with diminishing amounts on subsequent days, the total not to exceed from 100 to 200 cc. save under exceptional conditions, when even 500 cc. is warranted.

2. In malignant forms, coincident injections of antigangrenous and antistreptococcic serum are made.

3. Serotherapy will be increased in value by associated phylactic treatment with chloroform, given orally or administered as an anesthetic, or with methanamine, given intravenously.

4. In intractable cases further assistance should be drawn on through the use of epinephrine and strychnine.

AMESSE, Denver.

PREVENTION OF COMPLICATIONS IN VACCINATION FOR SMALLPOX. OPITZ, Bull. Assoc. internat. de pédiat. prevent. **4**:5, 1937.

Some account is given of the harmful symptoms consequent on vaccination. The symptoms may be the direct consequence of the operation, in which case a difference should be made between specific and nonspecific complications.

A large proportion of these complications are preventable; a smaller part can be avoided by indirect means. The number of inevitable cases is thus extremely small. These include cases of vaccinia generalisata and to a certain extent also cases of encephalitis. To combat these diseases physicians should be far more careful in passing children for vaccination. Unfavorable conditions should be more widely defined, and children with the following should certainly be excluded: (1) slight disorders of the digestive and respiratory systems and the predisposition to these difficulties, (2) nervous instability and spasmophilic tendencies, (3) rickets, (4) otitis media, (5) acute infectious diseases and (6) active tuberculosis (allergic children under 3 years of age should be regarded as in this class).

It is also possible to diminish the harmful consequences of vaccination by reducing the number of incisions to two and by using special bandages.

AMESSE, Denver.

TWO CASES OF POSTPOLIOMYELITIC SURGICAL RECONSTRUCTION. P. SANCHEZ TOLEDO, Cir. ortop. y traumatol., Habana **5**:87 (April-June) 1937.

Two cases of deformity of the shoulder following infantile paralysis are presented in which operative procedures were carried out with success.

HERRON, Monroe, La.

EPIDEMIOLOGY, PROPHYLAXIS AND TREATMENT OF POLIOMYELITIS. E. A. BERETERVIDE, J. de pediat., Rio de Janeiro **4**:551 (Dec.) 1937.

This is the first article in a review of this subject. SANFORD, Chicago.

PERTUSSIS ENCEPHALITIS. A. INVALDI, Rev. Soc. de pediat. de Rosario **2**:130 (Sept.) 1937.

The condition occurred in an 8 year old child on the tenth day of the disease. Spinal puncture showed only an increase in albumin. Recovery occurred.

SANFORD, Chicago.

DILUTING VEHICLE AND DOSAGE OF PROPHYLACTIC INHALANT AGAINST SCARLET FEVER IN CHILDREN. G. ISHIYAMA, J. Orient. Med. **27**:385 (Aug.) 1937.

Ishiyama studied three diluents for the preparation of an inhalant prophylactic against scarlet fever: (1) a 1 per cent solution of sodium chloride, (2) a 1 per cent solution of sodium bicarbonate and (3) a salt-soda solution (1 per cent each of sodium chloride and sodium bicarbonate). The effect of these three diluents on the formation of agglutinins in the blood was identical. The effect of the sodium bicarbonate solution and of the salt-soda solution was better than that of the sodium chloride solution on the formation of agglutinins in lung extract. In young rabbits the intratracheal injection of the concocted suspension with per kilogram dosage had the same immunologic effect as in mature animals.

KATO, Chicago.

ANTIGENICITY OF DIPHTHERIA TOXOID ADMINISTERED IN DIFFERENT FORMS. K. MANAKO, J. Orient. Med. **27**:455 (Oct.) 1937.

As tested on guinea pigs and rabbits, the diphtheritic toxoid precipitated with alum and calcium phosphate had the greatest antigenic power. The next greatest antigenicity was shown, in order of power, by alum-precipitated toxoid in suspension, calcium phosphate–precipitated toxoid, alum-precipitated toxoid in solution,

purified toxoid, acid-precipitated toxoid in suspension and acid-precipitated toxoid in solution. In contrast with the acid-precipitated toxoid, the supernatant fluid from the precipitation was found to be as effective as the original toxoid.

KATO, Chicago.

A NEW CULTURE MEDIUM FOR DIFFERENTIATING TYPES OF DIPHTHERIA BACILLI. G. ISHIMAYA, J. Orient. Med. **27**:477 (Oct.) 1937.

Ishimaya finds that the typing of diphtheria bacilli is greatly facilitated by the use of a new medium, made up of the following ingredients:

	Cc.
Agar, 2.5 per cent (*p*H 7.6)	10.0
Sodium glutamate, 10 per cent	0.5
Sodium tellurate, 0.8 per cent	0.5
Rabbit blood	1.0

On this medium diphtheria colonies for typing can be grown in from forty to forty-eight hours, whereas similar growths on McLeod's or Gundel-Tietz medium require much longer incubation.

KATO, Chicago.

MYOCARDITIS AND PERICARDITIS IN CONNECTION WITH GERMAN MEASLES. B. G. NORDENFORS, Nord. med. tidskr. **14**:2032 (Dec. 11) 1937.

A boy of 14 contracted German measles Jan. 6, 1937. From the second day on he had high fever and pains in the joints. On admission to the hospital January 15 he had a temperature of 40 C. (104 F.), a pulse rate of 100 and an increased rate of sedimentation of red blood cells; he suffered from pains but displayed no objective signs of joint disease, and he had no murmurs in the heart. Next day there were signs of pericarditis, and the electrocardiogram showed signs of myocarditis. After a temporary improvement, a relapse occurred a week later, with a large exudate, which had to be punctured. There was 400 cc. of sterile fluid containing a few leukocytes and lymphocytes. Rapid recovery followed, and the boy was discharged ten weeks after admission with normal findings for the heart.

WALLGREN, Göteborg, Sweden.

MEASLES ENCEPHALITIS. H. LILLIESTIERNA, Svenska läk.-tidning. **34**:1129 (Aug. 6) 1937.

This is a description of 5 cases of encephalitis complicating measles in children between 4 and 14 years of age. The neurologic symptoms began on the first or second day after the eruption and consisted in somnolence, which progressed in some of the cases to complete loss of consciousness, convulsions, marked clinical signs of meningitis in 3 cases and an increase in the cell and globulin content of the spinal fluid in all cases. Recovery occurred in all cases; in 4 it was complete; in the fifth case it was complicated with an organic lesion of the nervous system (congenital syphilis?), previously diagnosed, and in this case there remained difficulties in speech and walking.

WALLGREN, Götenborg, Sweden.

RESPIRATOR TREATMENT OF RESPIRATORY FAILURE IN INFANTILE PARALYSIS. R. BERGMAN, Svenska läk.-tidning. **34**:1467 (Oct. 22) 1937.

In 1930 patients with poliomyelitis in Sweden were for the first time treated in the respirator, but it was not until 1933 that this treatment began to be extensively used. At first the Drinker respirator was employed, but now Swedish physicians agree that the Swedish respirator constructed by Sahlin is the best. Bergman has treated 35 patients with respiratory failure, and 7 of them left the hospital living. Two of them will remain invalids for life, but the other 5 not only take care of themselves but at least partially earn their living. Of the 28 patients who died, 20 succumbed to circulatory failure, 5 to pneumonia and the last 3 to causes that had nothing to do with their poliomyelitis. The respirator

treatment lasted for less than three days in 21 cases, from three to seven days in 5 cases and more than thirty days in 5 cases. In the remaining 4 cases the need of treatment in a respirator was intermittent. Bergman emphasizes the need of a sufficient supply of respirators throughout the country and recommends that they be concentrated in a restricted number of centers. Patients in need of such treatment are now sent by plane for many miles to a respirator center.

WALLGREN, Göteborg, Sweden.

Acute Infectious Diseases

RELATIONSHIP OF SYDENHAM'S CHOREA TO OTHER RHEUMATIC MANIFESTATIONS. L. P. SUTTON and K. G. DODGE, Am. J. M. Sc. **195**:656 (May) 1938.

This analysis is only a part of a study made of 1,052 rheumatic children. A total of 467 records of children with chorea have been analyzed from a number of different angles. The authors draw the following conclusions:

Sydenham's chorea is not usually per se a serious condition. Approximately 20 per cent of patients who have had chorea as the only clinical manifestation of rheumatic infection come to have rheumatic heart disease. The child who begins his rheumatic career with chorea runs a 50 per cent chance of having heart disease develop. He runs a 50 per cent chance of having other rheumatic manifestations develop later, and if muscle and joint pains are included, a 75 per cent chance.

Emotional factors are no more important, and probably less so, in initiating an attack of chorea than preceding acute infection, including rheumatic polyarthritis.

Chorea should continue to be regarded not only as a manifestation but as a major manifestation of rheumatic infection.

HENSKE, Omaha.

OBSTRUCTIVE EMPHYSEMA AND ATELECTASIS IN INFLUENZA. W. SNOW and C. S. B. CASSASA, J. A. M. A. **109**:1887 (Dec. 4) 1937.

Snow and Cassasa discuss the pathologic and roentgen findings in influenza in young patients. They believe that the secretions produced by the action of the organisms of influenza and the associated secondary invaders cause by obstruction either a mechanical emphysema or atelectasis or both and that these phenomena should be anticipated in order to interpret the picture and treat the condition.

HEERSMA, Kalamazoo, Mich.

TREATMENT OF GONOCOCCIC INFECTIONS WITH SULFANILAMIDE. J. A. C. COLSTON, J. E. DEES and H. C. HARRILL, South. M. J. **30**:1165 (Dec.) 1937.

The authors find that sulfanilamide has great value in the treatment of gonococcic infection. In a series of over 80 patients with gonococcic infection of various types, 20 of whom were under the care of other observers, there was not a single patient in whom the infection progressed beyond the stage in which it was originally seen. Sulfanilamide seems to have a definite toxic effect on the gonococcus, but the exact mechanism of this effect is as yet not well understood. The authors are convinced that the best results are accomplished only by the administration of relatively large doses, at least in the early stages of treatment. They warn against indiscriminate use of the drug.

SCHLUTZ, Chicago.

"PRONTOSIL" IN TREATMENT OF MALARIA. R. A. HILL and M. H. GOODWIN JR., South. M. J. **30**:1170 (Dec.) 1937.

The authors find that prontosil (4-sulfamido-2', 4'-diaminoazobenzene hydrochloride, a derivative of sulfanilamide) is effective in treating patients infected with Plasmodium vivax and Plasmodium falciparum. This is especially true

when the patients have suffered previous attacks. The drug appears to be more useful in the treatment of chronic and malignant infections and is not so useful in the treatment of benign and initial infections.

SCHLUTZ, Chicago.

TETANUS TOXOID: ACTIVE IMMUNIZATION AGAINST TETANUS. M. FERNAN-NUNEZ, Wisconsin M. J. **37**:21 (Jan.) 1937.

The tetanus death rate of the population of the United States is recorded as 3 per hundred thousand. The missed cases make it actually much higher. The lethality rate in cases of tetanus is from 40 to 70 per cent.

The soils of the Hudson River valley are the most heavily infested in the United States. Wisconsin soil, because of the dairy industry, is more contaminated than the soil of other midwestern states. The dust of city streets contains tetanus organisms invariably. The organisms are destroyed readily by ordinary antiseptic measures, but the spores can withstand exposure to 5 per cent phenol for ten hours. To kill the spores, it is necessary to apply live steam at 120 C. for thirty minutes. The spores remain alive in street dust for years. The chief fraction of the tetanus exotoxin, a neurotoxin, is, with the exception of that of botulism, the most powerful poison known. Trismus neonatorum is the greatest single cause of infant mortality in the tropics. The incidence of trismus neonatorum is reduced to zero by giving the mother antitoxin before delivery. In general therapy 20,000 units of antitoxin are given intravenously (in an equal amount of 0.6 per cent saline solution), then 10,000 units intraspinally daily for three days and thereafter from 5,000 to 10,000 units daily intramuscularly for five days.

Active immunization with tetanus toxoid (made routine in the French Army in 1936) was carried on in 84 medical students by administering 1 cc. doses every three months. The reactions were negligible. The antitoxin content of the blood serum of 20 of these students, taken ten days after the second dose, was 0.25 unit per cubic centimeter; 0.1 unit is considered adequate protection against tetanus. Five months later the titer of the serum from 4 students was still 0.15 unit. A third dose jumped the titer to 0.35 unit per cubic centimeter.

It is recommended that active immunization with two doses of tetanus toxoid (0.5 cc. each) be given to those likely to be exposed (e. g., children, farmers, policemen, soldiers, sailors, athletes, stablemen and physicians). This should be followed by an additional dose each year and on possible exposure. The immunizing doses can be given in combination with typhoid-paratyphoid vaccine or, in children, with diphtheria toxoid.

JANNEY, Wauwatosa, Wis.

ANTITETANUS SERUM THERAPY. M. CAMNER, M. CAMNER and D. CUCOS, Bull. Soc. de pédiat. de Iasi **7**:81 (Oct.-Dec.) 1936.

The authors report on 5 children with tetanus, of whom 4 recovered. Large quantities of antitetanus serum were used in the treatment of each child, and the original wound was extensively cauterized. To 3 of the patients, chloroform was administered for twenty minute periods, two or three times. There are two theories to explain the effect of chloroform: that of Dufour, who thinks that under the influence of this drug the nerve cell is more susceptible to the detoxifying action of the serum, and that of Le Clerc, who thinks that the anesthetic mobilizes the fixed toxin. The authors prefer the intraperitoneal route for the administration of the serum.

LESLIE, Evanston, Ill.

SINUSITIS AND ITS COMPLICATIONS IN ACUTE INFECTIOUS DISEASES IN CHILDREN. W. GUMINSKI and F. KAPLANOWA, Pedjatrja polska **17**:73 (March-April) 1937.

The authors came to the conclusion that sinusitis in children is frequent, and that the complications of sinusitis during infectious disease are serious. As to treatment, the results in infants and small children are discouraging. It is most

important to promote drainage of the sinuses. Some authors have observed 100 per cent mortality in children with complications of sinusitis.

KRUPINSKI, Chicago.

STAPHYLOCOCCUS BACTEREMIA IN CHILDREN: A CLINICAL STUDY OF FORTY-THREE CASES. J. P. WU, Chinese M. J. **52**:807 (Dec.) 1937.

Of the 43 children with this disease admitted to the Peiping Union Medical College Hospital in the past sixteen years, over half were in the first 2 months of life. Prematurity was a common predisposing factor, as well as dysentery or streptococcic infection. The skin was the most common single site for the initial lesion. Treatment was entirely ineffectual, but prevention should be attempted by special care of the skin and respiratory tract. The mortality in children under 2 years of age was 100 per cent, and that for the whole group was 86 per cent.

NEFF, Kansas City, Mo.

NOTE ON A MALARIA SURVEY IN KIAO-CHIAO. M. N. ANDREWS and T. C. CHU, Chinese M. J. **52**:884 (Dec.) 1937.

A survey at the Public Health Station, Peiping, concerned school children mostly. Plasmodia, dominantly Plasmodium vivax, were found in 4.2 per cent of 7,766 examinations. In the autumn the percentage was 8, while in the spring it was 1.7, which was the lowest of the year.

NEFF, Kansas City, Mo.

Chronic Infectious Diseases

DOES OPERATIVE FUSION OF TUBERCULOUS JOINTS PRODUCE TUBERCULOUS MENINGITIS? F. L. LIEBOLT, Arch. Surg. **35**:1095 (Dec.) 1937.

Liebolt points out that during the twenty-three year period (from 1889 to 1912) before operative fusions came into use, when all tuberculous patients were treated conservatively, 1,398 persons with tuberculosis were admitted to the hospital, on whom no operation other than aspiration was performed. However, 149, or 10.6 per cent, of these patients died of tuberculous meningitis, an average of 6.5 deaths a year. During a similar length of time (from 1912 to 1935) during which operative fusion was performed, 1,752 patients with tuberculosis were admitted to the hospital, on whom 1,941 operations were performed. Only 23 of these patients, however, died of tuberculous meningitis. This is a percentage of 1.3 of patients admitted and of 1.1 of operations performed, with an average of 1 death a year. In 8 of the 23 cases of death occurring between 1912 and 1935, no operation was performed because of the patient's condition at the time of admission and during the stay in the hospital. If these 8 cases are eliminated, the percentage of deaths for the patients who were operated on drops from 1.1 to 0.77. Postmortem examinations were made on all but 4 of the 15 patients on whom operation was performed. The diagnosis of tuberculous meningitis was confirmed in each case. In only 1 patient was the fusion solid—a patient with tuberculosis of the spine; in 4 the status of the joint was not known, and in 18 fusion was not present. This, therefore, is evidence that lack either of operative or of natural fusion of a tuberculous joint is in many cases a predisposing factor to tuberculous meningitis. Surgical intervention in a case of a tuberculous joint does not produce tuberculous meningitis.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

THE VARIABILITY OF THE KAHN REACTION IN CHILDREN. HAROLD B. ROTHBART, J. Pediat. **11**:484 (Oct.) 1937.

Rothbart reports on 12 apparently nonsyphilitic children whose reaction to Kahn tests of the blood were positive on one or more occasions. Seven were girls and 5 were boys. In no case was there a family history suggestive of syphilis. None

of the children demonstrated any syphilitic stigmas. Four children gave weakly positive reactions, all but 1 of which became negative, and the remainder gave strongly positive reactions which subsequently became negative. Infection, either acute or chronic, was present in 11 cases. In 4 of the children febrile periods were associated with positive reaction. In 2 cases there seemed to be no relation between the degree of fever and the Kahn reaction. In 1 case the reaction became negative when the fever subsided. In another case the Kahn test on the spinal fluid remained positive but only by the presumptive method. Pathologic examination of the tonsils of 1 child revealed chronic infection, such as is seen in syphilis. The Levaditi silver-staining method demonstrated the presence of spirochetes which resembled morphologically Spirochaeta pallida but which in all probability were the spirilla of Vincent. Two other patients giving positive reactions died, but no evidence of syphilis was found at autopsy. The length of time the reaction may remain positive is uncertain. In 1 case it remained positive for six weeks; the patient was then not seen until a year later, at which time the Kahn reaction had become negative. Infection seems to have been the primary cause of the false reaction of these patients. Technical errors in carrying out the tests seem unlikely, for the laboratory personnel is under the direction of Dr. Kahn.

It has been suggested that the Wassermann and Kahn tests are merely a means of determining the amount of lipoproteolytic ferment present in the serum. It is thought that this enzyme is produced mainly by the lymphocytes and plasma cells stimulated to production by the lipoids of S. pallida. Kahn feels that while this may be true, other factors, biologic and physicochemical, as yet unidentified, play a significant role in producing positive reactions. These factors, though most frequently found in syphilis, may be present in other diseases or in abnormal functional states. Therefore, a positive reaction should not be considered absolutely pathognomonic of syphilis. Corroborative evidence is necessary. The author concludes with a plea against a hasty diagnosis of syphilis based on a positive reaction without any other evidence to support the diagnosis. Repeated serologic tests extending over a period of weeks should be made before treatment is begun.

RAUH, Cincinnati.

UNTREATED SERONEGATIVE MOTHERS OF SYPHILITIC CHILDREN: REPORT OF TWO CASES. J. R. WAUGH, J. Pediat. **11**:490 (Oct.) 1937.

Two cases of prenatal syphilis in children born of untreated mothers with negative Wassermann reactions of the blood are described. Of 78 mothers of children with prenatal syphilis seen during the years 1930 to 1936 inclusive, only 2 (2.6) had negative Wassermann reactions on admission or gave no history of a previous positive Wassermann reaction. A review of the literature shows that there is no difference of opinion as to the benign course of syphilis in women but that there is a difference of opinion as to whether pregnancy is the cause. Whether pregnancy had anything to do with the apparently spontaneous cure of syphilis in these 2 mothers cannot be determined.

FROM THE AUTHOR'S SUMMARY.

THE MANTOUX TEST: A STATISTICAL, CLINICAL, AND ROENTGENOLOGIC SURVEY OF 6,155 INFANTS AND CHILDREN OVER A PERIOD OF NINE YEARS. LEWIS A. SCHEUER and JACK R. KAREL, J. Pediat. **11**:670 (Nov.) 1937.

The Mantoux test was performed on 6,155 children in the New York Foundling Hospital from 1928 to 1937. There were 291 positive reactors, representing 4.7 per cent of the total number investigated. Eight per cent of the children were Negroes. Seventy-five (28.4 per cent) of 265 positive reactors had a definite history of exposure to tuberculosis (histories were not obtainable for the remaining 26 children). The mother was a source of infection for 89.3 per cent of these patients. Fourteen positive reactors (5.2 per cent) had clinical tuberculosis, and 8 of these (57.1 per cent) died of tuberculous infection. The youngest patient noted with a positive Mantoux reaction was 18 days old.

FROM THE AUTHORS' SUMMARY.

TUBERCULOSIS OF BONES AND JOINTS. FRANK E. JARDINE, Edinburgh M. J. **44**:173 (Nov.) 1937.

Primary tuberculosis begins in the glands of the neck, the hilus of the lung and the abdomen. Secondary lesions are located in the rapidly growing bones. There still exists some confusion in differentiating an infective granuloma of tuberculosis from one of actinomycosis.

The author reports 6 cases, in 4 of which the patients were children. A child aged 5 years had a tuberculous involvement of the eleventh and twelfth thoracic vertebrae. In this region the blood supply depends on the anterior branch of the anterior spinal artery; the disease develops at the point of maximum strain, namely, the junction of the fixed mobile parts of the spine. One should not treat this condition by the removal of the affected part, nor can the blood supply be improved. Usually operative splinting at this site is not advisable. Nature's attempt consists of collapse and osteosclerosis of the diseased vertebrae. Conservative measures are indicated, such as the application of a plaster shell to rest the spine and care in a sanatorium directed toward improving the general health.

The second patient, a boy aged 11, had tuberculosis of the hip joint. The region of strain in the hip joint is the angle between the head and the neck of the femur. It is here that tuberculous osteomyelitis develops, manifested by limping because of the close relationship of the psoas muscle. Cure of the osteomyelitis may come about within nine months, but usually, as in this case, the disease invades the joint capsule. As a result of effusion, the ligamentum teres becomes stretched and may constrict the artery and reduce the blood supply. Roentgenograms of the hip show that the head is eroded and is in danger of being completely destroyed.

A 10 year old child had tuberculosis of the knee joint. This condition should be suspected whenever a persistent unilateral swelling occurs in this location. The swelling is due to hydrops, commonly brought about by trauma of the synovial membrane. In the treatment a moderate amount of the fluid must be aspirated for the purpose of relieving the tension on the intra-articular ligaments. The blood supply to this joint is good, so that a favorable result may be obtained early, especially with the aid of the beneficial care at the sanatorium. The author describes what further operative treatment may be needed if there is erosion of the cartilage or thickening of the lower end of the femur.

A child aged 2 years had tuberculosis of the abdominal glands. The author states that ingested bacilli passing the tonsils may finally lodge in the mesenteric glands, usually producing no harm but in some instances causing tuberculous disease. Nature's method of giving rest to the active mesentery is by the production of peritonitis with ascites. The fluid of the disturbed abdomen should not be removed by laparotomy, for in many cases active tuberculosis follows such an operation. Conservative treatment, with the omission even of tapping, permitted this child to make an excellent recovery. The palpable glands disappeared.

NEFF, Kansas City, Mo.

TUBERCULOSIS OF THE CENTRAL NERVOUS SYSTEM, WITH ESPECIAL REFERENCE TO TUBERCULOUS MENINGITIS. A. R. MACGREGOR and C. A. GREEN, J. Path. & Bact. **45**:613 (Nov.) 1937.

Macgregor and Green declare that the ideal method for the isolation of tubercle bacilli from the cerebrospinal fluid is the utilization of both direct culture and inoculation of guinea pigs. If direct culture is adopted, the Löwenstein-Jensen medium is likely to be of more service than the mediums used more commonly as a routine. Of a series of 80 cases of tuberculous meningitis, the infecting organism was of the human type in 76 per cent and of the bovine type in 24 per cent. Of these cases, 2 per cent occurred in the first six months of life, 14 per cent in the first year and 81 per cent within the first decade. The human type of organism was responsible for 91 per cent of cases of primary thoracic infection terminating in tuberculous meningitis, and the bovine type, for 9 per cent. By

contrast, the two types were responsible for approximately equal numbers of cases in which the disease terminated in meningitis with an initial focus of infection in the abdomen. It was reasonably certain that the exudative meningitis had arisen from a localized lesion. In 1 case the lesion responsible was in the spine; in the others it was in the brain or meninges. The localized lesions in the central nervous system took the form of caseous nodules in the substance of the brain and cord, tubercles or deposits of tuberculous exudate in the meninges or choroid plexus and areas of tuberculous meningo-encephalitis. In 25 cases of tuberculosis without meningitis examination was made for evidence of infection of the central nervous system. In 11 of 24 cases localized tuberculous lesions were observed in the brain. In 10 of 20 specimens of cerebrospinal fluid tubercle bacilli were demonstrated. In 45 cases in which there were symptoms of cerebral or meningeal irritation and a reaction to the tuberculin test, the cerebrospinal fluid was examined for tubercle bacilli and other evidence of tuberculous infection. In 3 cases tubercle bacilli were isolated, and in 2 others the cerebrospinal fluid showed cytologic changes strongly suggestive of tuberculous infection. In no case did fatal tuberculous meningitis develop.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

SYNDROME OF OBESITY IN CHILDREN WITH NEURAL INVOLVEMENT AND HEREDITARY SYPHILIS. PAUL GIRAUD and BOUDOURESQUE, Bull. Soc. de pédiat. de Paris **35**:304 (May) 1937.

A boy aged 12 years had adiposogenital dystrophy, some narrowing of the fields of vision and congenital syphilis. A girl aged 8 years had obesity, paralytic mydriasis of the pupils due to involvement of the oculomotor nerves and congenital syphilis. Glandular therapy had no effect, and it is believed that the glandular dyscrasias were caused by neural lesions affecting the endocrine system. The commonest etiologic agents which produce neural lesions affecting the endocrine glands are syphilis and intracranial birth injuries.

BENJAMIN, Montreal, Canada.

PULMONARY TUBERCULOSIS IN INFANTS: CONSIDERATION OF SIX CASES. F. TORELLI, Lattante **8**:535 (Sept.) 1937.

Torelli reports 6 cases of fatal pulmonary tuberculosis, the patients being children from 2 to 9 months of age. The infection came from the parents, each of the children having lived in an environment of maximum exposure to contagion. Prophylactic treatment by early removal from the source of the contagion is imperative in such cases.

HIGGINS, Boston.

THE VALUE OF LOOKING FOR TUBERCLE BACILLI IN THE STOOLS FOR THE DEFINITE DIAGNOSIS OF INFANTILE TUBERCULOSIS. P. PUCCIONI, Riv. di clin. pediat. **35**:912 (Oct.) 1937.

Cultures of material taken from the stools of 28 tuberculous infants were made for tubercle bacilli. The bacilli were found in only 3 cases, while studies of the sputum and gastric contents had demonstrated the bacilli in 15 cases. Therefore, Puccioni concludes that the procedure is not of much value in the diagnosis of infantile tuberculosis.

HIGGINS, Boston.

THE FRAGILITY OF THE RED CELLS OF CHILDREN WITH TUBERCULOSIS: A STUDY USING THE METHOD OF SIMMEL. F. AUXILIA and C. TASCHINI, Riv. di clin. pediat. **35**:1049 (Dec.) 1937.

The fragility of the red blood cells of 50 children with various types of tuberculosis was determined according to the method of Simmel. In nearly every case the red blood cells of the tuberculous children were more readily hemolyzed by hypotonic salt solutions than were the red blood cells of normal children. This

diminished resistance may be due to tuberculous toxemia, to changes in the physical chemistry of the red blood cells, to the physicochemical conditions of the plasma, to the reaction of the bone marrow to the disease or to an abnormal cholesterol-lecithin equilibrium.

HIGGINS, Boston.

EXPERIENCES WITH EPITUBERCULOSIS. H. FAZ TABIO, Arch. de med. inf. **6**:421 (Oct.-Dec.) 1937.

The prominent features of epituberculosis are the absence of pathognomonic signs and the scarcity of bacilli. Adequate treatment in proper surroundings will shorten the course of the disease.

SANFORD, Chicago.

PERIARTERITIS NODOSA MUTILANS: REPORT OF A CASE. VRANOVA, Časop. lék. česk. **75**:76 (Jan. 17) 1936.

Vranova gives a short résumé of the literature and reports a case in detail. A boy aged 4 years was sick for a year after an attack of measles and two severe attacks of sore throat with infection of the cervical glands. The periarteritis was of the pseudorheumatic, dermatomyopolyneuritic or septic type. The disease progressed with an undulating type of septic temperature. The following symptoms were present: Pain in the joints and muscles; edema of the extremities, the face and the torso; exanthema maculopapulosa; adenitis; foci in the skin, simulating erythema multiforme; both superficial and deep hemorrhagic areas of the skin and underlying tissues, and obliteration of arteries, with infarcts of the skin and mutilating necrosis of the terminal phalanges of several fingers. The leukocyte count varied from 20,000 to 45,000, with a shift to the left; eosinophilia was present. The Pirquet reaction was positive, and cultures in Löwenstein's medium showed the presence of tuberculosis. The cause may be a combination of tuberculosis and capillary hypersensitivity or allergy, though the bacillemia per se may be explained simply on the basis of the mediastinal tuberculosis.

STULIK, Chicago.

SIMPLE EDEMA OF THE SCROTUM IN CONGENITAL SYPHILIS: REPORT OF THREE CASES. J. W. MU, Chinese M. J. **52**:377 (Sept.) 1937.

This rare condition is not accompanied by inflammation of the skin or of the structures within the scrotum. The author has been unable to find a record of similar cases.

Mu's patients were 3 infants aged 2 months. The parents had syphilis. The infants showed the following symptoms: snuffling; lesions of the long bones; lesions of the lips, the palms, the soles and the anus; and enlargement of the liver and spleen. Antisyphilitic treatment cleared up the symptoms.

NEFF, Kansas City, Mo.

REPORT OF MANTOUX TESTS ON 34,781 JAPANESE AND MANCHOUKUO SCHOOL PUPILS IN THE KWANTUNG LEASED TERRITORY. J. IIO and others, J. Orient. Med. **26**:1103 (June) 1937.

Mantoux tests were done on 22,815 Japanese and 11,966 Manchoukuo school children, a total of 34,781 subjects. Of the Japanese children, the majority lived in the city of Dairen and gave 39.33 per cent of positive reactions, while the small number living in suburban communities gave 36.75 per cent. Of the children living in Manchoukuo, the urban inhabitants gave 64.30 per cent of positive reactions and the suburban inhabitants 46.81 per cent. Among the urban inhabitants who gave positive reactions there was a slight predominance of the male sex, while among the suburban class the girls gave a slightly higher percentage of positive reactions.

KATO, Chicago.

SENSITIVITY TOWARD TUBERCULIN IN VARIOUS TYPES OF TUBERCULOSIS IN CHILDREN. N. LANDORF, Acta pædiat. **20**:1, 1937.

This is the report of studies which have been carried out during the last few years in Wallgren's Clinic in Göteborg, Sweden. After 1,018 children had been classified according to the type of tuberculous infection which they presented, serial Mantoux tests were carried out in such a way as to determine the smallest amount of tuberculin which would produce a positive reaction in the individual members of the various groups. The two principal classifications were "active tuberculosis" and "healed intrathoracic tuberculosis;" the first group included 697 children and the second 321 children. As judged by the results of Mantoux titration, sensitivity to tuberculin was highest in those patients who were suffering from fresh primary infection and from cavitating tuberculosis; the lowest degree of sensitivity was found in cases of miliary tuberculosis and tuberculous meningitis; other varieties of tuberculous infection occupied intermediary positions from the point of view of sensitivity. Eight hundred and fifty-five of the 1,018 children were tested by the Pirquet scarification technic in addition to the Mantoux method; of these, 157 failed to react to the percutaneous method. Further studies of this discrepancy suggested that it was due either to the inherent lack of sensitivity of the Pirquet test or to technical errors in its execution. The conclusion is expressed that the Pirquet test is not the equivalent of the Mantoux test performed with 0.1 mg. of tuberculin but at best approximates the results to be expected from the intracutaneous method when 0.01 mg. of tuberculin is employed.

McCUNE, New York.

ABSCESS IN SPONDYLITIS TUBERCULOSA. C. P. H. TEENSTRA, Maandschr. v. kindergeneesk. **6**:476 (Sept.) 1937.

This paper offers an extensive discussion of tuberculous abscess in cases of spondylitis. Special stress is laid on the fact that the abscess must be regarded as an active tuberculous extension of the original process in the bone. Spondylitis generally is benign when early and careful treatment is applied. The abscess also is important for the making of an early diagnosis. The author points to the difference in prognosis between closed and open fistular tuberculosis; the last-mentioned form usually can be prevented by a careful treatment of the abscess. This treatment is exhaustively discussed.

VAN CREVELD, Amsterdam, Netherlands.

THE INDICATION FOR TREATMENT OF PULMONARY TUBERCULOSIS IN A SANATORIUM. B. H. VOS, Nederl. tijdschr. v. geneesk. **81**:4684 (Oct. 2) 1937.

The principal indication for treatment of pulmonary tuberculosis in a sanatorium is the finding of tubercle bacilli in the sputum when the infection is fresh, because this as a rule proves the existence of a cavity. Treatment in a sanatorium is, furthermore, the best way of teaching the patient hygienic living. The social indication depends on the circumstances in which the patient is living. Treatment in a sanatorium is also indicated in cases of chronic tuberculosis with symptoms of reactivity and often in cases of pulmonary involvement which spreads only slowly and shows but little activity, especially when cavities have been found. When hemorrhages from the lungs are present treatment in a sanatorium may save the patient's life. The author presents an extensive discussion of the circumstances in which such treatment is absolutely or provisionally contraindicated.

VAN CREVELD, Amsterdam, Netherlands.

COLOR OF THE EYES AND TUBERCULOSIS. H. SANDRA, Nederl. tijdschr. v. geneesk. **81**:5401 (Nov. 6) 1937.

In examining the eyes of 2,017 persons who came to his office to be examined for tuberculosis the author paid special attention to the existence of an eventual

relation between tuberculosis and the color of the eyes. He examined 1,736 blue-eyed persons and 218 brown-eyed persons. He found some indication of a somewhat greater frequency of tuberculosis among the brown-eyed persons, but he is of the opinion that a much larger amount of material is necessary for certainty.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

IRON-COBALT TREATMENT OF PHYSIOLOGIC AND NUTRITIONAL ANEMIA IN INFANTS. K. KATO, J. Pediat. **11**:385 (Sept.) 1937.

The effect of feeding cobalt on the bone marrow of healthy animals was studied. This element was found to stimulate the bone marrow, causing progressive hyperplasia of all cellular elements and a consequent discharge of erythrocytes into the circulation. Cobalt was used in conjunction with iron in treating animals in which a simple nutritional anemia had been produced. The animals showed rapid restoration of erythrocytes and hemoglobin to normal levels. This effect was probably due to a catalytic action of the cobalt salt, for no evidence of its presence was found in the blood by spectroscopic examination. Of all the organs of the body, the liver was found to store cobalt in the greatest concentration. Cobalt was used in treating infants for nutritional anemia in a dosage approximately one tenth of that of iron; from 25 to 50 mg. was administered daily, in combination with 0.5 Gm. of assimilable iron. The red cell count increased approximately 250,000 weekly; the hemoglobin content, 0.75 Gm. per hundred cubic centimeters of blood, and the hematocrit reading, 1.5 per cent.

Kato suggests the use of cobalt as an adjunct to iron therapy during only the first two to three weeks of active treatment because its action in hemopoiesis is that of a catalyst. After from 12 to 13 Gm. of hemoglobin per hundred cubic centimeters of blood has been reached, the medication may be entirely withheld or the administration of iron continued alone. No alarming pathologic changes can be produced by cobalt in the vital organs of the body if the element is used in the recommended dosage and for the recommended time. RAUH, Cincinnati.

THROMBOCYTOPENIC PURPURA HEMORRHAGICA: TWO CASES TREATED WITH PARATHYROID HORMONE AND CALCIUM GLUCONATE. M. L. AINSWORTH, S. D. EDELMAN and R. I. FRIED, J. Pediat. **11**:559 (Oct.) 1937.

A patient with idiopathic thrombopenic purpura and one with thrombopenic purpura following an acute exanthem thought to have been scarlet fever were successfully treated with solution of parathyroid and calcium gluconate. The authors suggest that perhaps the solution of parathyroid makes the blood calcium more available for the clotting cycle, as postulated by Howell. Prompt cessation of the purpuric manifestations occurred simultaneously with increase in the blood calcium and the platelet count.

RAUH, Cincinnati.

THE ANEMIC CHILD. H. W. JOSEPHS, J. Pediat. **11**:607 (Nov.) 1937.

The approach to the subject of anemia may be either (1) to look on the various forms of anemia as the result of definite anatomic changes which constitute the disease of which the blood picture is a superficial aspect or (2) to look on the anemia as due to disturbances in physiologic processes which have been brought about by various etiologic factors. This paper considers the following processes: (1) the synthesis of hemoglobin, (2) hemopoietic activity, (3) hemolysis and (4) disturbance in maturation.

Deficiency of hemoglobin may result from a lack of material for its formation or because of a failure of synthesis. The tendency at present is to regard

hypochromic anemia as synonymous with anemia due to a deficiency of iron, but mere lack of iron is not the only factor involved, for failure of synthesis may be quite as important.

Hemopoietic activity, or the capacity of the hemopoietic tissue to respond to stimulation or to the need for blood replacement, is essential to a cure of anemia, so that a determination of reticulocytes should be a necessary part of any study of the blood. The term "hypoplastic anemia" is used to designate inadequate regeneration. Lack of adequate regeneration may occur in (*a*) aplastic anemia, (*b*) replacement of the bone marrow and (*c*) lack of adequate stimulation. There seems little doubt that hemopoietic activity is subject to some sort of control, though the mechanism governing this control is unknown. There is a tendency to an aregenerative form of anemia in diseases involving the spleen and reticulo-endothelial system. Probably the commonest cause of such hypoplasia is infection.

The third process of importance is hemolysis. The recognition of increased hemolysis when this process is predominantly responsible for anemia is usually not difficult, though jaundice may be absent, especially in infancy.

Disturbance in maturation, the fourth process discussed, occurs (1) when marked stimulation of the normal marrow follows hemorrhage or occurs at the onset of the recovery phase in acute hemolytic anemia, (2) when the bone marrow has been seriously reduced by an encroachment, with extramedullary formation of blood following this, or (3) when there is a disturbance in erythropoiesis interfering with maturation, the degree of immaturity depending on the depth of the disturbance. There is a close relationship between disturbance in maturation and increase in hemolysis. Josephs believes it is impossible to separate the two and feels that one should speak of the hemolytic-erythroblastic group of anemias. The presence of a process affecting one element of the blood often affects others as well. Increase in regeneration may be accompanied by increase in the number of white cells, and erythroblastosis may be accompanied by marked immaturity of the white cells, a condition to which the name "pseudoleukemia" has been given. This picture is found in septic infections, particularly in small babies. "Hypoplasia" may be present in infections but also occurs in the majority of cases in which the immaturity is at the so-called megaloblastic level.

The relations between the processes are constantly shifting with progression or remission of the disease, as new etiologic factors cause new disturbances or as improvement in one process may unmask some other process, previously unsuspected. Each case must be evaluated as a whole, and each characteristic must be considered in relation to the light it may throw on the nature of the disturbances and on the etiologic factors that play a part in creating the disturbances.

RAUH, Cincinnati.

THE DIAGNOSIS OF HEART DISEASE IN CHILDREN. W. S. LOVE JR., M. Clin. North America **21**:1291 (Sept.) 1937.

The conditions in which difficulties of diagnosis most commonly exist are discussed in this paper. Congenital heart disease is considered from a modern standpoint and is classified clinically as (1) the acyanotic group, in which no shunt is present; (2) the potentially cyanotic group, in which an arteriovenous shunt exists, (3) the cyanotic group, in which the shunt is venous arterial.

Heart disease acquired in childhood is almost invariably rheumatic in origin. Rheumatic infection in early life, however, is usually atypical in its symptoms, and its true nature may at times be determined only on the evidence of the cardiac involvement. If a clearly defined valvular lesion is present, it may be assumed that the damage to the heart occurred at some time previous to its discovery. The evaluation of a systolic murmur at the apex, transmitted or not, presents a troublesome problem. If such a murmur is transient or occurs only with exercise or excitement and without other signs of cardiac disease, it is probably of little significance. However, if it occurs in a child with a rheumatic history,

with reversal of the character of the first and second sounds at the apex and with accentuation of the second pulmonic sound, it probably indicates mitral stenosis.

EUGENE H. SMITH, Ogden, Utah.

CONGENITAL DEXTROCARDIA: REPORT OF TEN CASES. L. K. EMENHISER, South. M. J. **30**:1055 (Nov.) 1937.

The patients were 8 females and 2 males, all white persons. Eight had the usual mirror type of congenital dextrocardia, with transposition of the abdominal viscera. One had congenital dextrocardia with the thoracic aorta descending to the left side of the vertebral column, without the transposition of the abdominal viscera and unaccompanied by other serious anomalies. Another showed the thoracic aorta descending on the right side of the vertebral column without the transposition of the abdominal organs but accompanied by other serious anomalies.

The electrocardiograms made in the cases of congenital dextrocardia with transposition of the abdominal viscera showed the pathognomonic sign of inversion of all waves in lead I and transposition of leads II and III.

The electrocardiograms made in the cases of congenital dextrocardia without transposition of the abdominal viscera did not show the pathognomonic signs described.

SCHLUTZ, Chicago.

AORTIC ANEURYSM IN CHILDHOOD: CASE REPORT, WITH SOME GENERAL REMARKS ON THE DESIRABILITY OF REPORTING RARE CASES. J. F. PILCHER, Texas State J. Med. **23**:3734 (Sept.) 1937.

Pilcher calls attention to the rarity of this disease and gives a complete autopsy report. He makes a plea for more complete reports of unusual cases.

MOORE, Dallas, Texas.

PREVENTION OF DISABILITY. A SYMPOSIUM: RHEUMATIC HEART DISEASE IN CHILDHOOD. H. E. MARSH, Wisconsin M. J. **36**:906 (Nov.) 1937.

Two per cent of all school children are afflicted with rheumatic heart disease. Heart disease is of rheumatic origin four times out of five in persons under 20 years of age, two times out of three in persons in the third decade of life and more than half the times in persons in the fourth decade. The causation is not known and cannot be prevented, but the outlook of those who have rheumatic heart disease depends largely on their care.

The symptoms are often too vague for early diagnosis. The most typical lesion is mitral stenosis, and yet those who have it frequently deny that they had at any previous time chorea or rheumatic fever.

The pulse rate gives the best information as to the cardiac state. If in the absence of fever the pulse rate while the child is asleep is about the same as the rate when the child is awake, activity of the disease can be generally presumed. Should the rate of the alert pulse be from 10 to 20 beats more than the sleeping pulse, the acceleration is probably of nervous origin. A gradual quickening of both the sleeping and the alert pulse rates indicates recrudescence of active infection.

Further enlargement of the heart, changing murmurs and involvement of other valves point to low grade cardiac inflammation. Subcutaneous nodules or active chorea do likewise. The sedimentation rate of the red blood cells, if other acute fevers can be excluded, is of assistance in diagnosis. Murmurs may not be obvious during acute endocarditis, being delayed until cicatricial changes occur. Fluoroscopic, roentgen and electrocardiographic examinations often clarify vague situations.

When the disease is in an active stage, the treatment consists in avoiding physical exertion and nervous excitement—everything else is subordinate. Absolute rest in bed should continue for from two to three weeks after the temperature

has become normal and has remained so without medication and until the pulse has returned to normal and is strong.

In the convalescent stage the patient's activities begin with sitting up in bed, then in a chair for a half hour increasing to two hours gradually. Walking is carefully started, with occasional two week periods when activity is at a standstill.

Foci of infection should be eradicated.

During the inactive period a thorough follow-up system is essential, with play and work being fitted to physical ability and a return to activity anticipated.

JANNEY, Wauwatosa, Wis.

THE CHEMISTRY OF PHOSPHATID LIPOIDOSIS. P. H. TEUNISSEN, Ztschr. f. physiol. Chem. **248**:142 (Aug.) 1937.

Schematic Representation of Lipoidosis

↓	↓	↓
Phospholipids	Cerebrosides	Cholesterol
Niemann-Pick disease	Gaucher disease	Essential xanthomatosis
Amaurotic family idiocy of Tay-Sachs type		Hand-Schüller-Christian disease
		General xanthomatosis of bones

The liver and spleen from a 6 month old infant with Niemann-Pick disease were analyzed for lipids. As controls were examined 3 spleens from 3 normal children, 12, 8 and 10 to 12 months old, as well as a spleen from a patient with Gaucher disease, a specimen which had been in solution of formaldehyde since 1905. The liver from a 3 month old infant was examined. The steps in the analysis are described in detail.

The findings in regard to the normal spleens agree closely with those of other observers. The spleen of the infant with Niemann-Pick disease contained 7.66 Gm. of lecithin per hundred grams of dry tissue, while the normal spleens averaged 1.60 Gm. The sphingomyelin content of the spleen of the infant with Niemann-Pick disease was also greatly increased, being 22 Gm. as compared with a normal content of 3.5 Gm. per hundred grams of dry tissue. The free cholesterol was normal, but the cholesterol ester was increased. The liver of the infant with Niemann-Pick disease showed lecithin and especially sphingomyelin greatly increased as compared with the normal. There was also a great increase in the free cholesterol, while an actual decrease was noted in the combined cholesterol, the ratio of free to combined cholesterol being 44.4 : 1, compared with 1.1 : 1 in the normal liver.

The spleen of the patient with Gaucher disease showed the lecithin and sphingomyelin contents little changed. There was, however, a large quantity of crystals typical of kerasin, which composed 14 per cent of the dry substance of the spleen. There was also a slight increase in the free cholesterol in the spleen of this patient. Teunissen believed it was significant that tissues which had been fixed in solution of formaldehyde for many years could be analyzed and give such satisfactory results.

HANSEN, Minneapolis.

THE NUMBER OF ERYTHROCYTES AND THE PERCENTAGE OF HEMOGLOBIN IN THE BLOOD OF NEWBORN CHILDREN. B. ANDERSEN and G. ORTMANN, Acta med. Scandinav. **93**:410, 1937.

For each of 43 newborn infants—all less than 24 hours old—a red blood cell count was made, and the percentage of hemoglobin and the packed red cell volume were determined. Cutaneous and venous blood showed the same values and variations.

The erythrocyte counts showed much greater variations than those of adults, similarly the percentages of hemoglobin; the hemoglobin content of the individual red blood cell was definitely greater 33.6 micromicrograms (in adults, 29 micromicrograms), as was the size of individual cells, so that the hemoglobin percental content of the cell was the same as in adults.

The total blood volume would have to be determined at the same time to prove that the present day conception that "acclimatization" of the fetus to the lower oxygen tension in utero is the cause of this difference from what is found in adult life.

KAJDI, Baltimore.

CHANGES IN THE SEDIMENTATION RATE OF ERYTHROCYTES IN STORED CITRATED BLOOD AS AN AID TO DIAGNOSIS OF MALIGNANT TUMORS AND LYMPHOGRANULOMA. L. KOSTER, Acta med. Scandinav. **93**:420, 1937.

The sedimentation rate of citrated blood was determined by Westergren's method immediately and one, two, three, four, five, six and twenty-four hours after being drawn.

The blood of 100 normal persons and 460 patients with benign tumors and inflammations was found without exception to show a decrease in sedimentation rate of at least 20 per cent after twenty-four hours. This is called the "lag" reaction.

In the blood of 106 of 112 patients suffering from malignant tumors and in all of 14 patients with lymphogranuloma this reaction was absent; in most cases the sedimentation rate was even higher after twenty-four hours than at the start and in the rest at least the same.

If the blood of a patient is diluted with an equal volume of the same patient's citrated plasma, the different behavior of the two groups becomes even more marked.

Plasma sodium showed parallel changes, increasing with the increase in sedimentation rate, while the potassium varied in the opposite sense; so Koster explains this phenomenon by reabsorption of the potassium by the red blood cells.

KAJDI, Baltimore.

PAROXYSMAL TACHYCARDIA WITH PARTIAL ATRIOVENTRICULAR BLOCK IN A GIRL OF EIGHT. C. MAARSSÖ, Hospitalstid. **80**:1140 (Oct. 12) 1937.

The child was first seen March 30, 1937. She then had had for a year periodical crises of cardiac palpitation and dyspnea following exercise and fatigue. She was somewhat cyanotic. The heart rate was 172 and irregular. Over the middle of the precordium was an inconstant systolic or presystolic murmur. The left border of the heart was at the anterior axillary line. The blood pressure was between 60 and 90 mm. of mercury. The Wassermann test was negative. The liver was not enlarged. The electrocardiogram showed the P wave negative in all leads, the ventricular complex normal, with slight right preponderance, and a partial atrioventricular block with steadily increasing conduction time. At some examinations no block was demonstrable. The outcome of the disease is unknown. The case is considered to be one of paroxysmal tachycardia produced by pathologic stimuli at the atrioventricular node. The partial block is regarded as a phenomenon of exhaustion and not as the result of an anatomic lesion of the bundle of His.

WALLGREN, Göteborg, Sweden.

THROMBOPENIC PURPURA IN A NEWBORN INFANT. N. NORDMARK, Nord. med. tidskr. **14**:1882 (Nov. 13) 1937.

A boy born at full term, breast fed, presented on the trunk and legs the second day after birth a rash of pinhead-sized purpuric spots. The thrombocytes were 36,000 per cubic millimeter. The petechiae increased in number during the following few days and then disappeared. The general state of health was good. There was no bleeding from the mucous membranes. The baby was discharged from the maternity hospital at the age of 9 days healthy. The thrombocyte count was then 376,000.

WALLGREN, Göteborg, Sweden.

THROMBOPENIC PURPURA IN AN INFANT. J. STRÖM, Nord. med. tidskr. **14**:1882 (Nov. 13) 1937.

A premature boy with a birth weight of 1,820 Gm. fell ill at 4 months of age with diarrhea, and ten days later blood was noted in the stools and purpuric spots appeared in the skin. When first seen by Ström, three days later, he had numerous small petechiae all over the body and splenomegaly. The thrombocytes numbered 70,000 per cubic millimeter; the bleeding time was five minutes; capillary resistance was lowered; there was no retraction of the blood clot; the clotting time was five minutes. Recovery occurred after some weeks.

WALLGREN, Göteborg, Sweden.

Diseases of Nose, Throat and Ear

EARLY DETECTION AND TREATMENT OF DEFECTIVE HEARING IN CHILDREN. H. NEWHART, J. A. M. A. **109**:1620 (Nov. 13) 1937.

Newhart enumerates the reasons for the lag in detection of deficiencies of hearing and the principles and methods of their detection both privately and on a large scale in schools and the state. These tests, especially the audiometric test, have disclosed much higher percentages of hearing deficiencies than were formerly found. Their discovery is of value in personal, social, economic and therapeutic lines. The pediatrician should aim to discover these impairments of hearing in the infant and preschool child as well as to eradicate any of the listed causes before damage to hearing has progressed.

HEERSMA, Kalamazoo, Mich.

INFECTION OF THE NASAL ACCESSORY SINUSES IN CHILDREN. E. A. LOOPER, M. Clin. North America **21**:1323 (Sept.) 1937.

All children having chronic colds in which nasal symptoms are predominant should have a careful investigation of their sinuses. A skilfully made and well interpreted roentgenogram is the most valuable diagnostic aid. Transillumination is unreliable and misleading. In obscure cases diagnostic puncture of a sinus may be necessary. The most common complication is orbital abscess. Meningitis and abscess of the brain are not common complications, and when they occur they usually result fatally.

In most cases sinus infection in children yields to proper local treatment. In only a small number are operative procedures required. Looper advises the use of warm saline sprays, followed by the application of 2 per cent silver nitrate or 20 per cent argyrol and an emollient. Suction is a valuable method of removing secretions. In a few cases a sinus may require puncture and irrigation, but only exceptionally are more radical measures indicated.

EUGENE H. SMITH, Ogden, Utah.

THE FUNCTION OF THE TONSILS AND THEIR RELATION TO THE AETIOLOGY AND TREATMENT OF NASAL CATARRH. I. GRIFFITHS, Lancet **2**:723 (Sept. 25) 1937.

Griffiths is assistant throat surgeon to the British Postgraduate Medical School and to Queen Mary's Hospital for the East End, London.

He states that there seems to be a physiologic enlargement of the lymphatic tissues between the ages of 4 and 6 and between the ages of 13 and 15.

He feels that the accepted indications for tonsillectomy are open to criticism and that removal of the tonsils does not necessarily bring improvement in middle ear disease, snoring or nasal catarrh. A study of 5,000 children suffering from diseases of the nose and throat showed that 385 had infection of the accessory nasal sinuses. Sinusitis was more frequent in children who had had tonsillectomy than in those whose tonsils were intact.

An experimental study (with instillations of india ink into the sinuses of dogs and cats) of the lymphatic drainage of the tonsils and sinuses suggested that the

function of the tonsils was to receive lymphatic drainage from the sinuses and to excrete bacteria into the throat. In no circumstances should tonsils be removed in treatment for nasal catarrh. LANGMANN, New York.

RELATION OF THE EAR, NOSE AND THROAT TO THE DISEASES OF CHILDREN. B. MORGAN, Proc. Roy. Soc. Med. **30**:1415 (Sept.) 1937.

When an infant receiving a correct and sufficient diet fails to thrive or suffers from some gastrointestinal disorder, an infection must be sought. The common infections arise from the upper respiratory and the urinary tract and from the skin. Infections of the upper respiratory tract vastly preponderate. The Continental and American authorities have insisted that almost constantly infection of the ear in the infant results from nasopharyngitis and have discussed the relationship between otitic infection and gastroenteritis. Morgan holds that silent otitis media is not specific to gastroenteritis, as he found it in the course of many of the acute diseases. But it is the relationship between infections and gastroenteritis that he discusses. Is the infection of the ear simply a terminal event which may occur in many diseases? Is it a secondary effect from the spreading of vomitus up the eustachian tube? Or may it be a primary cause or a complicating factor of the disease? Mastoid disease in the small infant is difficult to diagnose. Nasal sinus disease is another frequent complication of the infection of the upper part of the respiratory tract, which may cause continued pyrexia, recurrent headache and chronic cough. Frequently the coughs are dry and associated with croup. When the nasal discharge is free, the cough is loose.

In asthmatic and bronchiectatic patients, Morgan advises operation on the sinus although the result may be disappointing. The view of the majority is that the whole respiratory tract is simultaneously infected.

In concluding his paper Morgan discusses the relationship between tonsillitis and the triad of arthritis, chorea and carditis. WILLIAMSON, New Orleans.

ADENOID VEGETATIONS AND OTITIS. M. LEVY-DEKER, Rev. méd.-sociale de l'enf. **5**:341 (Sept.-Oct.) 1937.

Without a reference or a case report Levy-Deker indulges in four pages of generalizations about the association of adenoids and otitis media. The description of the anatomic and physiologic aspects of adenoids is brief and orthodox. One cannot deny that hypertrophied adenoids may interfere with drainage from the middle ear and that chronic otitis in very young children may be cleared by adenoidectomy, and one must agree that infants and young children with large adenoids may have more otitis media than those with small vegetations. But when the author asserts that congestion of adenoids caused by dentition favors otitis media and that local resistance is lowered by chronic infection of adenoids, this abstracter can no longer keep pace. DIETRICH, Beverly Hills, Calif.

A CASE OF PRIMARY CROUP. B. BELFORT, Ann. de pediat., São Paulo **1**:99 (Nov.) 1937.

This was a case of laryngeal diphtheria, as the organisms were recovered. The laryngoscope was used, and treatment was by administration of oxygen and 110,000 units of antitoxin. SANFORD, Chicago.

TOPICAL APPLICATION OF COD LIVER OIL IN TUBERCULOSIS OF THE LARYNX. A. S. ILYICH, Vrach. delo **19**:567, 1937.

Ilyich discusses the rationale of the topical application of cod liver oil in tuberculosis of the larynx and presents in detail 2 cases.

Cod liver oil has been reported by various observers to have a favorable effect on the healing of poorly granulating surfaces by stimulating the production of

granulation tissue, an effect which is believed to be due to its content of vitamin A. Likewise, it appears that cod liver oil exerts an unfavorable if not a bactericidal action on the tubercle bacillus as do other oils of animal origin.

Cod liver oil was therefore used by Ilyich, in combination with menthol because of the known analgesic and soothing properties of the latter. The laryngeal instillation of menthol is a widely accepted method of symptomatic treatment in tuberculosis of the larynx. Instillations of a 3 per cent solution of menthol in cod liver oil in amounts of from 2 to 5 cc. were done daily or biweekly, the patient being requested to hold his head back for from one to two minutes following the treatment.

Rapid improvement followed in the majority of cases, as judged by the disappearance of symptoms, such as pain and dysphagia, and by the diminution of the local hyperemia and gradual healing of the affected surface.

The author believes that the systematic topical application of cod liver oil with 3 per cent menthol in tuberculosis of the larynx may bring about definitely favorable results and that it is an adequate method of treatment, especially when a more radical form of therapy is not indicated.

BODER, Los Angeles.

TONSILLECTOMY: A REVIEW OF ONE THOUSAND CASES. C. P. YANG, Chinese M. J. **52**:389 (Sept.) 1937.

Yang reports facts concerning the indications for, and the technic of, operation, the condition of the tonsils on section and the postoperative results. About 55 per cent of the patients were between 6 and 15 years of age; few were less than 3 years of age. One infant of 15 months had greatly enlarged tonsils, with mouth breathing and with undernutrition. Those who suffered most from general systemic infections comprised 3 per cent of the patients; their tonsils were not enlarged but often contained many crypts. There was definite enlargement of the glands of the neck in 45 per cent of the patients. Secondary hemorrhage is the most common postoperative complication and was present in most of the cases, but patience in the operative care will insure against such a happening, for never was there a disastrous result.

There were only 2 instances of postoperative pneumonia, such a sequel being usually prevented by the use of the Rose position and a painstaking technic. The follow-up reports indicate that 77 per cent of the patients were well and that 14 per cent were improved, especially those who had previously been affected with frequent coughs, colds and tonsillitis. When the operation was done to remove a focus of infection or to affect the cure of a systemic disease, the results were usually disappointing.

NEFF, Kansas City, Mo.

HEMATURIA AFTER TONSILLECTOMY. H. RASMUSSEN, Hospitalstid. **80**:28 (Nov. 23) 1937.

The urine of 117 patients was observed after operations on their tonsils, and in the urine of 5 of these patients slight hematuria was found. Six patients who had had nephritis previously did not show any erythrocyturia after the operation.

WALLGREN, Göteborg, Sweden.

RETROPHARYNGEAL ABSCESS WITH FATAL BLEEDING. T. LEEGARD, Norsk mag. f. lægevidensk. **98**:1421 (Nov.) 1937.

Leegard reports a case of retropharyngeal abscess in a boy 12 years of age. A fortnight after the beginning of the disease the abscess perforated spontaneously. The perforation was accompanied by fatal bleeding.

WALLGREN, Göteborg, Sweden.

Diseases of Lungs, Pleura and Mediastinum

Observations on the Treatment of Asthma and Related Conditions with Suprarenal Cortical Extract (Cortin). L. E. Prickman and G. A. Koelsche, J. Allergy **9**:158 (Jan.) 1938.

The authors conclude that comparatively large doses of an extract of adrenal cortex, intravenously administered, supplemented by excessive amounts of sodium chloride, given by mouth, was of little or no specific benefit to a group of patients who had asthma and certain related conditions.

Hoyer, Cincinnati.

The Differential Diagnosis of Pneumonia in Childhood. A. H. Parmelee, M. Clin. North America **22**:55 (Jan.) 1938.

Attention is called to some of the peculiarities of pneumonia as it occurs in childhood by the citation of 5 cases. Vomiting is frequently an initial symptom, as of other infections at this age. Abdominal pain is common and is usually due to pleurisy. The expiratory grunt is almost pathognomonic of pneumonia. Definite physical changes in the lungs may elude detection for some time after the onset of characteristic symptoms. Fever in bronchopneumonia may not maintain the high level characteristic of lobar pneumonia, and cough and general fatigue may be the outstanding symptoms. A frequent cause of unexplained fever is otitis media, and daily examination of the ears should not be neglected. Chills occur infrequently in infants and young children and are usually due to pyelitis, especially in girls. The next most common cause is pneumonia. Newborn infants will often show no febrile reaction to an infection, particularly when this infection is virulent and overwhelming. At this age progressive weakness, slight cyanosis, rapid respirations and a few rales may be the only evidences of extensive bronchopneumonia. In young infants infected with the influenza bacillus the inflammation spreads rapidly downward to the bronchioles, causing partial or complete obstruction of the lumens. Some air reaches the terminal alveoli, but little can escape, and hyperinflation or emphysema results. On physical examination one finds asthmatic breathing, hyperresonance and expiratory dyspnea. The prognosis for these infants is always poor.

Eugene H. Smith, Ogden, Utah.

The Urinary Excretion of Pneumococcus Polysaccharide in Lobar Pneumonia. R. Cruickshank, J. Path. & Bact. **46**:67, 1938.

The specific polysaccharides of pneumococcus types I, II and III are excreted in the urine of the majority of patients with lobar pneumonia due to these three types, and the polysaccharide of each type may be demonstrated by a precipitation reaction. This urinary precipitation test has only a limited value as a method for the early serologic typing of lobar pneumonia, as the first specimens of urine examined gave precipitation in only one fifth of the cases of type I and one half of the cases of type II infection. The detection of the polysaccharide in the urine early in the infection has, however, a grave prognostic significance, since the mortality in such cases was around 40 per cent, whereas, of patients whose urinary specimens were persistently negative, less than 2 per cent died. The specific substance continues to be excreted in the urine during the patient's convalescence, and in explanation of this phenomenon it is suggested that the polysaccharide as antigen is gradually dissociated from the antibody and slowly excreted by the kidneys.

From Author's Summary. [Arch. Path.]

Asthma in Children. D. L. Barlow, M. J. Australia **1**:4 (Jan. 1) 1938.

The possibility that asthma is an etiologic factor in bronchitis of childhood should always be kept in mind. Environmental factors are important in producing asthma. Great care should be exercised in diagnosing septic conditions of the

nose and sinuses, because the picture produced by allergy is so similar to that of infection. In treatment there should be exhaustive search for offending allergens and desensitization whenever possible. Change of environment is helpful, and there should be increased efforts at removal of offending allergens from the air on a large scale.

TENNEY, Madison, Wis.

PERIHILAR AND PERISCISSURAL SHADOWS IN THE EVOLUTION OF CHRONIC NON-BACILLARY DISEASE IN CHILDHOOD. F. TISSOT, Arch. de méd. d. enf. **41**:26 (Jan.) 1938.

Among children in preventoriums, surrounded by modern facilities for prompt adaptation to the best hygienic regimen, signs of primary tuberculous infection as shown by roentgenograms and cutireactions usually disappear within a few months. While a diagnosis can usually be based on the latter factors, there are rare cases in which a negative reaction to tuberculin serves to check an otherwise certain opinion. Three observations are recorded, with illustrations; all the patients exhibited suspicious roentgenologic phenomena without the characteristic skin reaction, and all were subsequently shown to suffer from lymphatism and neuro-arthritism, which produced, through chronic peribronchovascular infiltration, the picture of pseudotuberculosis.

AMESSE, Denver.

AMOUNT OF OXALIC ACID IN THE BLOOD IN SOME DISEASES OF THE RESPIRATORY TRACT IN CHILDREN. C. GUALAZZINI, Riv. di clin. pediat. **36**:23 (Jan.) 1938.

There was an increase in the oxalic acid in the blood of children with acute bronchopneumonia, acute lobar pneumonia or unresolving pneumonia. This was highest at the time of the crisis; then it began to diminish slowly. When the child had recovered, the oxalic acid was at a normal level. The age of the child, the body temperature and the extent of the pulmonary involvement did not have any direct relation to the amount of oxalic acid. The toxicity of the patient, causing changes in metabolism, was probably responsible for the increase of oxalic acid in the blood.

HIGGINS, Boston.

SMALL NODULES IN THE LUNGS. G. PESCI and G. CASSINELLI, Riv. di clin. pediat. **36**:33 (Jan.) 1938.

The cases of 2 children with bronchopneumonia, one of them following measles, are reported. In each, roentgen films showed small shadows in the lung fields typical of miliary tuberculosis. The tuberculin test was positive in each child. However, both children recovered from the pneumonia, and the miliary shadows gradually disappeared from the roentgen films. One must be guarded in making a diagnosis of miliary tuberculosis on roentgen evidence alone.

HIGGINS, Boston.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

LYMPHOID HYPERPLASIA OF THE APPENDIX. S. H. GRAY and C. J. HEIFETZ, Arch. Surg. **35**:887 (NOV.) 1937.

Gray and Heifetz reviewed the pathologic reports of 14,000 appendixes. They found that 51 showed definite lymphoid hyperplasia. The clinical symptoms and signs were studied. It was found that the symptoms simulated those of mild appendicitis and occurred most frequently in the postpubertal years and early adulthood. The lymphoid hyperplasia of the appendix was probably caused by a parenteral infection. A theory is presented indicating the possible etiologic relationship between lymphoid hyperplasia and acute appendicitis. A preoperative diagnosis is seldom made. No follow up studies were undertaken to determine to what extent symptoms were relieved following operation.

KAISER, Rochester, N. Y.

NONSPECIFIC MESENTERIC LYMPHADENITIS. S. ROSENBERG, Arch. Surg. **35**:1031 (Dec.) 1937.

Mesenteric lymphadenitis is described as a disease entity. It is described from experience with 75 cases in which Rosenberg operated. He makes the following classification of this disease: (1) chronic mesenteric lymphadenitis, (2) acute mesenteric lymphadenitis, (3) acute fulminating mesenteric lymphadenitis and (4) acute suppurative mesenteric lymphadenitis. The problem of diagnosis is similar to that of diagnosing acute and chronic appendicitis. Abdominal operation is usually performed because it is impossible to rule out acute or chronic disturbance of the appendix. No definite etiologic factor is known. In the author's series only a few cases of tuberculous adenitis were encountered. It was suspected that in most of the cases in which operation was performed the condition was secondary to some respiratory infection. Follow-up letters elicited information indicating that only one third of the patients were relieved of abdominal pain after laparotomy.

CLINICAL ASPECTS OF INFANTILE DIARRHOEA. E. D. COOPER, Arch. Dis. Childhood **12**:339 (Dec.) 1937.

The clinical findings in 300 cases of diarrhea and vomiting in infancy are reviewed. Artificial feeding appears to be the most important etiologic factor. Parenteral infection was present in 40 per cent of the cases; it did not have as marked an influence on the mortality rate as might be expected. The mortality rate varied inversely with the age and state of nutrition. The morbid anatomic changes in the bowel found post mortem did not in many cases bear any relation to the severity of the symptoms. The value of administration of fluid in the treatment is emphasized.

KELLY, Milwaukee.

CHEMICAL CHANGES IN THE BLOOD IN INFANTILE DIARRHOEA AND THE EFFECT OF INTRAVENOUS ADMINISTRATION OF FLUID. E. D. COOPER, Arch. Dis. Childhood **12**:349 (Dec.) 1937.

The protein of serum and the nonprotein nitrogen and chloride of whole blood were estimated in cases of acute gastroenteritis and chronic diarrhea. In the former the values for protein, nonprotein nitrogen and chloride all tended to be high while in the latter low values for protein and chloride were frequently obtained and the nonprotein nitrogen generally fell within normal limits. The significance of these findings is discussed, and it is suggested that in acute gastroenteritis there is a loss of water from the circulating blood and that the water leaves the blood stream without its full quota of chlorine. In chronic diarrhea it appears that water enters the blood without its full quota of chlorine. As a result of injections of saline solution and of dextrose characteristic alterations occur in the serum protein of normal infants. In infants with acute gastroenteritis these alterations are much less marked, and it is concluded that the blood plasma remains diluted for much longer than in the infant without dehydration. The results of adding calcium gluconate to the injected fluid suggest that in infantile diarrhea calcium gluconate may be of some benefit in accelerating the movement of fluid from the circulation to the tissue spaces.

KELLY, Milwaukee.

CHANGES IN THE WATER AND CHLORIDE CONTENT OF THE TISSUES IN INFANTILE DIARRHOEA AND OTHER CONDITIONS. E. D. COOPER, Arch. Dis. Childhood **12**:359 (Dec.) 1937.

The chloride and water contents of the tissues are greater in infants than in adults. No definite loss of chloride or of water from the tissues of infants who die of diarrhea and vomiting can be demonstrated. In infants with diarrhea and in those with peritonitis there occurs as a result of administration of saline

solution a marked fixation of both chloride and water in the tissues. An important depot for this storage appears to be muscle. The younger the infant the greater is its capacity to fix chloride and water following the administration of saline solution. No definite relation between the chloride and water contents and the duration of illness or the terminal temperature is apparent. Patients with the most severe malnutrition often exhibit high chloride and water contents and also greater retention of these substances after the administration of saline solution. It is suggested that increased fixation of chloride in tissues after saline solution has been injected is due to renal insufficiency. KELLY, Milkaukee.

COELIAC DISEASE WITH A CONDITIONED VITAMIN DEFICIENCY RESEMBLING BUT NOT TYPICAL OF PELLAGRA. R. LIGHTWOOD and V. SMALLPIECE, Proc. Roy. Soc. Med. **31**:71 (Dec.) 1937.

A boy of 15 months had been well until the age of 5 months when a rash appeared on the trunk which spread to the limbs and persisted. He had been treated at an outpatient clinic for seborrheic eczema, and because he was losing weight he was admitted to the hospital. The child was breast fed for six months and given orange juice and halibut liver oil; he lived in excellent surroundings. When the authors first saw him, he was 11 months old. His color was high and his skin dry and eczematous. There was hypotonia with kyphosis. The abdomen was very large. The stools were large and offensive, and there were two daily. There were corneal changes. The Wassermann reaction was negative. Roentgen examinations, urinalyses, fecal examinations, progress and treatment are then reviewed in the report, which is also accompanied by pictures of the patient and discussions as to diagnosis. WILLIAMSON, New Orleans.

TWO CASES ILLUSTRATING THE USE OF INTRAVENOUS GLUCOSE CURVES TO TEST LIVER FUNCTION. R. WILSON, Proc. Roy. Soc. Med. **31**:74 (Dec.) 1937.

1. A boy aged 8 years was admitted to the hospital on account of an enlarged liver, jaundice and a plasma phosphatase reading of 51 units. After clinical recovery a test of tolerance for levulose administered by mouth showed no improvement of function, and a test of tolerance of dextrose administered intravenously (Ross technic) showed gross impairment. The curves were improved after an intravenous injection of liver extract.

2. A girl aged 8 years was admitted on account of malaise, anorexia and frequent nosebleed. The liver and spleen were both enlarged. An intravenous dextrose tolerance curve showed definite impairment of function, which was markedly improved after a dose of liver extract, given intravenously.

WILLIAMSON, New Orleans.

DISEASES OF THE BILIARY TRACT IN CHILDHOOD. C. RADU, L. HABER, J. PETRESCO and G. STOINESCO, Arch. de méd. d. enf. **40**:779 (Dec.) 1937.

It is commonly accepted by writers and clinicians that diseases of the biliary passages, both congenital and acquired, are extremely rare. When found, either accidentally, as in the course of surgical operations, or at autopsy, the exciting cause is usually the colon or the typhoid bacillus.

In 1934 Guerstein and Reydermann published an exhaustive report on angiocholecystitis in children and asserted that the disease is much more common than ordinarily believed. This study stimulated the present authors to search for the disorder in their own clinic and within two years they have observed it clinically in 26 patients, the observations being verified by duodenal drainage. In 6 other patients suspected of having it the tube could not be employed. Complete histories from this series are attached and some conclusions concerning the etiologic factors, clinical evolution and treatment are offered. AMESSE, Denver.

Is Operation Necessary in Every Case of Hypertrophic Stenosis of the Pylorus in an Infant? R. Baranski and M. Bussei, Rev. franç. de pédiat. **13**:480, 1937.

The authors feel that even in definite cases of tumor of the pylorus operation is not always indicated. If the loss of weight is not rapid and if there is no oliguria and the general condition of the infant is good, medical treatment may be of avail. Three cases are reported in which excellent results were obtained without operation.

Leslie, Evanston, Ill.

Oxalic Acid in Diseases of the Gastrointestinal Tract of Children. G. Frola, Lattante **8**:639 (Dec.) 1937.

Oxalic acid was determined in the blood of 8 infants with acute gastroenteritis, 12 infants with ileocolitis and 7 infants with dyspepsia. Parallel determinations of the blood sugar were also made. In the infants with dyspepsia and ileocolitis the oxalic acid of the blood was within normal limits. In 4 of the 8 infants with acute gastroenteritis there was an increase in the oxalic acid but no comparable change in the blood sugar.

The conclusion was drawn that an increase in the oxalic acid of the blood is not due to increased fermentation in the intestines but rather to abnormal metabolic changes, especially in the liver.

Higgins, Boston.

A Foreign Body (Coin) in the Esophagus. C. A. Cruz Bustillo, J. pediát. de Santiage de Cuba, 1937, p. 151.

A 3 year old child had a copper coin (described as a Belgian franc) in her esophagus for approximately four and a half months before attempts were made to remove it. Two efforts at extraction by means of the esophagoscope failed because the coin could not be visualized, being restrained and hidden by esophageal mucosa. Under general anesthesia, esophagotomy was performed and the coin removed. No sutures were used in the esophageal wound or in the muscle and fascia of the neck, a gauze drain being employed. The esophageal wound closed on the tenth postoperative day. Liquid nourishment by mouth had been permitted immediately after the operation.

Kaliski, San Antonio, Texas.

Treatment of Aphthous Stomatitis with Vitamin C. S. Fritz, Kinderärztl. Praxis **8**:504 (Dec.) 1937.

Daily injection of 0.15 Gm. of a pure vitamin C preparation, together with oral administration of vitamin C in tablet form or as a powder, improved aphthous stomatitis remarkably in from two to three days.

Heymann, Cleveland.

Diverticula in the Small Intestine. A. Bodarwé, Röntgenpraxis **9**:403 (June) 1937.

Diverticula of the intestine may be of congenital origin, or they may be acquired. In the congenital type all layers of the intestine are found in the walls of the diverticulum, while in the acquired variety only the mucosa, the submucosa and the serosa are present in the walls of the sac; the muscularis is absent. Of the various regions of the alimentary tract the jejunum is the least common site of diverticula. The occurrence of the condition in a woman aged 67 is reported. Long-standing symptoms suggestive of disease of the gallbladder led to roentgen examination, in the course of which a diverticulum of the jejunum was demonstrated. Operation was successful. The diverticulum was of the congenital type.

McCune, New York.

INTERPOSITION OF THE COLON: A CONTRIBUTION TO THE STUDY OF ABDOMINAL PAIN DURING CHILDHOOD. A. WINDORFER, Ztschr. f. Kinderh. **5**:129 (Oct. 14) 1937.

Interposition of the colon has been described in adults but not previously in children. Windorfer reports a case in an 8 year old girl who had had repeated attacks of colicky abdominal pain. During one of these attacks, clinical examination revealed absence of liver dulness over the lower right side of the chest and presence of dulness posteriorly. Roentgen examination revealed the colon shadow (identified by haustra) below the right side of the diaphragm. The condition was accompanied by hepatoptosis, enteroptosis and hypotonic musculature. The differential diagnosis includes all conditions causing abdominal pain, as well as diaphragmatic hernia, subphrenic gas abscess, gas accumulation secondary to a perforation of the wall of the stomach or of the intestine and situs inversus viscerum.

SIEMSEN, Chicago.

TREATMENT OF HIRSCHSPRUNG'S DISEASE BY MEANS OF OPERATIONS OF THE SYMPATHETIC NERVOUS SYSTEM. W. F. SUERMONDT, Maandschr. v. kindergeneesk. **6**:383 (July) 1937.

The author describes 2 cases of Hirschsprung's disease in which the condition occurred in girls aged respectively 13 and 17. In both cases the disease was successfully treated by lumbar sympathectomy.

VAN CREVELD, Amsterdam, Netherlands.

ATRESIA OF THE OESOPHAGUS WITH AN OESOPHAGOTRACHEAL FISTULA. J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **6**:419 (Aug.) 1937.

The author presents a description of 3 such cases, with extensive discussion of the cause, diagnosis, prognosis and eventual treatment of this congenital malformation. He states that the condition should be regarded as a retardation in development.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

THE CAMPAIGN AGAINST EPILEPSY. W. G. LENNOX, Am. J. Psychiat. **94**:251 (Sept.) 1937.

After discussing the medical, social and economic aspects of epilepsy, Lennox makes the following recommendations for its control: (*a*) Society must be made aware of the magnitude of the problem. There are over one-half million persons in the United States suffering from seizures. The public must recognize the present neglect of those in whom epilepsy is in an incipient stage. It must also recognize the necessity of an improvement in the facilities for extensive research. (*b*) Among physicians there must be a wider diffusion of knowledge and a harder search for new knowledge, as well as a will to work together toward a common goal—the end of epilepsy.

JAHR, Omaha.

ACUTE INFECTIVE POLYNEURITIS IN CHILDHOOD. M. S. HECHT, J. Pediat. **11**: 743 (Dec.) 1937.

Hecht reports 7 cases of extensive flaccid paralysis in young children. The cases are thought to belong to a group described in the literature under a number of names, among which are "acute infective polyneuritis" and "radiculoneuritis." The characteristics of the group are: (*a*) There is widespread, frequently ascending flaccid paralysis or paresis tending to affect proximal muscles in the extremities as much as or more than distal ones. The involvement is symmetric and widespread, not patchy. (*b*) There is frequent involvement of the facial nerves

—sometimes of the lower cranial nerves but never of the higher ones. (*c*) Sensory disturbances may be present or absent. If present, they are less prominent than the motor phenomena. Muscle tenderness occurs occasionally. (*d*) Disturbances of the bowel and bladder may be present but are relatively mild and transient. (*e*) The spinal fluid shows an increase in globulin with little or no increase in cells. (*f*) Fever, if present, is mild. (*g*) There is often a history of mild illness, usually respiratory, preceding the onset of paralysis. (*h*) Unless death occurs from respiratory failure early in the disease, recovery usually takes place without permanent paralysis.

Insufficient pathologic data have been accumulated to establish a firm anatomic foundation for this disease. In the cases in which autopsy has been performed the spinal roots and peripheral nerve roots bore the brunt of the attack, but lesions have also been described in the meninges, posterior root ganglions, gray matter of the cord and even the cerebral cortex. Descriptions of the lesions by different observers vary considerably. Until more information can be obtained it is better to regard acute infective polyneuritis as a syndrome of possibly multiple origin rather than a disease entity. There is no specific therapy. Orthopedic care is important for the prevention of contractures.

RAUH, Cincinnati. [FROM THE AUTHOR'S SUMMARY]

RECOVERY OF A CHILD AFTER COMPLETE REMOVAL OF A CEREBELLAR TUMOR WITH HEMIPLEGIA. W. R. LIPSCOMB and J. G. LOVE, Proc. Staff Meet., Mayo Clin. **12**:689 (Nov. 3) 1937.

An 11 year old girl, previously subjected to decompression, was operated on for an astroblastoma of the cerebellum, measuring 7 by 10 cm. Complete recovery followed.

MILLER, South Bend, Ind.

TUMOUR OF THE SPINAL CORD IN A CHILD AGED 2½ YEARS. SPECIMENS. C. P. LAPAGE and D. E. POOLE WILSON, Proc. Roy. Soc. Med. **30**:1185 (Aug.) 1937.

A child of 2½ years was brought to the hospital with the history that for several days she had been listless and had cried if touched or picked up. She was unable to walk. Eighteen months prior to this she complained of pain in her left hand, and the mother noticed that she did not use it. At that time a roentgenogram was taken, and as it showed nothing the doctor at the hospital said the pain was due to rheumatism. On the ninth day in the hospital, following an attack of hyperpyrexia, death occurred. The authors report the results of the physical examination, the progress of the condition and the observations at autopsy. The pathologist reported that the histologic features of the tumor were those of a malignant ependymoma of the spinal cord. The growth extended from the fourth cervical to the fifth thoracic segment, lying on the anterior aspect of the cord, apparently situated between it and the arachnoid.

WILLIAMSON, New Orleans.

INJURIES TO THE BRAIN IN EPILEPTIC FITS AND THEIR RELATION TO BRAIN FINDINGS IN IDIOCY AND LITTLE'S DISEASE. W. SCHOLZ, Chinese M. J. **52**:450 (Sept.) 1937.

Prof. W. Scholz, director of the Institute of Brain Pathology, Munich, Germany, gave an address at a conference in Shanghai, which is summarized on the editorial page of this Chinese journal. Epilepsy still occupies an obscure field in medicine, its pathologic anatomy unsolved. However, either lobular atrophy or sclerosis has been discovered in the brains of most epileptic patients. Scholz seeks the explanation of epileptic attacks occurring before there are clear signs

of mental defect or paralysis. In examinations of 200 brains of persons who were epileptic, no evidence of a chronic progressive disease process was found.

Most of these autopsies were made in children in the first ten years of life. There were examples of fresh damage from convulsions. If death comes late, characteristic features are lost before autopsy takes place; such features are found within from eighteen to twenty hours after an initial attack or, if there have been several attacks, within two or three days after these attacks. If the patient had lived, there should have been, as a result of the intense and protracted circulatory disturbance, disseminated necrosis of ganglion cells or incomplete necrosis of tissue, going on to scarring and contraction.

The material discussed by Scholz came from children with epilepsy in whom idiopathic epilepsy, idiocy and cerebral paralysis had been observed. The mental or physical defects did not occur at the beginning of the illness but had been preceded by epileptic attacks in earlier childhood. Damage from convulsions must be included with trauma sustained at birth, cerebral paralysis and encephalitis in the list of causes of feeblemindedness acquired in early childhood. If the lesions of the brain are frequent, of sufficient size and suitably located, epilepsy may run a protracted course consistent with an idiopathic type. However, unmistakable signs of damage to the brain may also come into the clinical fixture.

NEFF, Kansas City, Mo.

CASE OF EPILEPSY WITH HEMIANOPIA (STURGE-WEBER DISEASE). P. SELANDER, Svenska läk.-tidning. **34**:345 (March 5) 1937.

A boy of 7 years, on commencing school, was found to have impaired sight. He was sent to an ophthalmologist. In 1928 he had an epileptic seizure. Observation in the hospital did not disclose any clinical signs of an organic lesion. In 1931 he had another epileptic attack. Examination of the eyes now showed bilateral atrophy of the papillae and hemianopia on the right. In 1936 there were the same symptoms and signs. A distinct hazelnut-sized calcification was demonstrable on the left side of the skull, corresponding to the occipital lobe of the cerebrum. At operation it was found that the calcification was localized to a hemangiomatous tumor, which was extirpated. Recovery followed.

WALLGREN, Göteborg, Sweden.

SPASMUS NUTANS. G. ÖSTERBERG, Ugesk. f. laeger **99**:806 (July 29) 1937.

Spasmus nutans is characterized by rhythmic movements of the head, often combined with torticollis and nystagmus. The symptoms usually begin in the winter time and when the patients are between 6 and 12 months old. The syndrome never begins after the third year of life. The prognosis is good. Four typical cases are reported in infants from 6 to 13 months old. Two cases of a similar syndrome are reported in children of 8 and 4 years, with organic lesions of the eyes and nervous system; in the latter, the symptoms had begun at from 1 to 2 years of age.

WALLGREN, Göteborg, Sweden.

MEDICINAL THERAPY OF INCREASED INTRACRANIAL PRESSURE. A. C. DE VET, Nederl. tijdschr. v. geneesk. **81**:4385 (Sept. 11) 1937.

In increased intracranial pressure two components should be clearly distinguished: increased pressure of the cerebrospinal fluid (measurable by physical methods and associated with a definite clinical syndrome) and so-called brain pressure (German *Hirndruck*, not measurable physically but associated with a well known clinical picture). The appearance and the symptoms of the patient with increased intracranial pressure are briefly reviewed. Subsequently the different methods of lowering intracranial pressure are discussed: the intravenous administration of hypertonic salt or dextrose solution and the oral and rectal use of concentrated solution of magnesium sulfate. Attention is drawn to the

fact that the medical methods in most cases (especially in those of tumor of the brain) are used in combination with other methods to lower intracranial pressure (decompressive trepanation; roentgen treatment), but under certain circumstances they may save a life. VAN CREVELD, Amsterdam, Netherlands.

TRYPTOPHAN REACTION IN CEREBROSPINAL FLUID. A. W. GRIEP, Nederl. tijdschr. v. geneesk. **81**:5610 (Nov. 20) 1937.

Fifty spinal fluids from different patients were examined. The tryptophan reaction is positive when the protein reactions are positive. The reaction is not specific for meningitis tuberculosa. VAN CREVELD, Amsterdam, Netherlands.

Psychology and Psychiatry

RESTLESSNESS IN CHILDREN. P. M. LEVIN, Arch. Neurol. & Psychiat. **39**:764 (April) 1938.

Levin points out the fact that restlessness in children is associated with mental deficiency, suggesting that it is due to a deficiency of the frontal lobe; or, more specifically, that it is associated with the "syndrome of the prefrontal region." He also points out that restlessness is sometimes found in normal children and feels that then it is due to "psychologic disturbances." BEVERLY, Chicago.

NEED OF A MENTAL HYGIENE PROGRAM FOR THE CHILDREN OF INDIANA. H. B. METTEL and E. E. WELSCH, J. Indiana M. A. **31**:21 (Jan.) 1938.

The Indiana State Board of Health has provided a mental hygiene program in cooperation with the Indiana State Medical Association, social service groups, and school and community interests. An effort is made to study the child and his environment and recommend treatment through existing local agencies. A plan is being formulated to place added emphasis on psychiatric teaching at Riley Hospital in cooperation with the Indiana University School of Medicine.

MILLER, South Bend, Ind.

THE INVALID REACTION IN CHILDREN. L. KANNER, J. Pediat. **11**:341 (Sept.) 1937.

The invalid reaction is the habit of complaining about somatic discomfort in the absence of evidence of organic disease. Approximately 5 per cent of all children referred to the psychiatric service of the Harriet Lane Home were sent because of some hypochondriac manifestation. Many of these children had been treated for years for various organic conditions. Kanner lists the complaints and describes the attitudes of some of these children. The majority of the chronic complainers belong either to the group of pampered or to the group of insecure children. The pampered children start out with capriciousness in regard to food, bedtime strategies and irregularity of toilet habits. The attention of the family has become focused on the bodily functions, following which the child's own attention is focused on these functions, and he uses anorexia, insomnia and elimination as tools for maintaining this attention. In the case of the insecure child, as when a new baby arrives in the home and there is need of proof of parental affection, the same tactics may be used. The child does not suddenly decide to complain about headaches or backache. Invariably there is an empiric basis for these complaints. The experience may have been provided by a previous illness during which the child discovered the power sickness gives him over those around him, and he may use this later as a means of escape from unpleasant tasks and experiences. An example furnished by another person may be the basis for this reaction. Not less than 53 per cent of the hypochondiac children

seen at the Harriet Lane Home had fathers and mothers who themselves were chronic complainers. In some instances the child may become the parent's hypochondriac organ. The difficulty begins with the parent's hypochondriasis concerning the child, who eventually comes to consider himself an invalid.

Another potent factor in the development of the invalid reaction may be the iatrogenic, or physician-determined, factor. The diagnostic scares and ambiguities of the physician, often misinterpreted by the parents and the child, make of the latter a chronic invalid. The use by the physician of what Kanner calls diagnostic "swear words" borrowed from the psychiatric vocabulary such as "nervous," "neurotic," "psychoneurotic," "neuropathic" and "psychopathic" often terrifies the parents. To them these words indicate the presence of organic disease, and the result is overprotection and overindulgence of the child.

There is always a basis for the invalid reaction, and the recognition of this reaction should lead to a search for the source. Treatment must be preceded by an understanding of the child, of the family attitude and of the situation responsible for the condition. Treatment must be more than asserting that nothing is wrong with the child. The parents and the child should be interviewed separately. Both must be convinced that the child is physically well and informed of the factors which have led to the invalid reaction. The situation underlying the reaction must be changed or made more tolerable, and the domestic sick room atmosphere must be driven out of the home. At the same time the child must resume the life of a healthy, active child. The doctor should pay a visit to the home the day after these recommendations to convince himself that they are being followed and to reemphasize them if necessary. Regular follow-up work with the child must be continued for some time.

The prophylaxis of invalidism begins at the beginning of life. Superstitions and faulty notions about prenatal influence and bugaboos of heredity must be dispelled. The parents must be guided in matters of nutrition, elimination and general habit training. If the practice of pampering, coddling and retardation of the development of self dependence can be suppressed early and if a healthy attitude toward the physical and mental development of the child is maintained in the home during the first two years of the child's life, a great deal may be accomplished in the prevention of hypochondriac reactions. The prevention of children's invalidism is primarily the domain of the pediatrician.

RAUH, Cincinnati.

PSYCHOLOGIC CARE DURING INFANCY. R. M. BAKWIN and H. BAKWIN, J. Pediat. **12**:71 (Jan.) 1938.

The pediatrician should give not only clinical advice but psychologic guidance during infancy and childhood. During infancy, when mental growth and development are extremely rapid, psychologic advice and prophylaxis are as important as clinical and nutritional care. The Bakwins discuss and offer suggestions for the management of children in regard to the following problems: formation of proper eating habits, prevention of anorexia, prevention and treatment for thumb sucking, development of good sleeping habits, training for rectal and vesical control, discipline, disorders of speech, hand preference, intelligence testing and parental attitudes.

RAUH, Cincinnati.

THE ROLE OF THE FAMILY IN THE MORAL DEVELOPMENT OF CHILDREN. E. PICHON, Rev. méd.-sociale de l'enf. **5**:321 (Sept.-Oct.) 1937.

This rather interesting paper discusses in some detail the attempts of the mother, the father and the state to shape the moral development of juveniles. The conclusions notwithstanding, there runs through the paper a feeling of pessimism, not shared by workers in the same field in this country.

DIETRICH, Beverly Hills, Calif.

Diseases of the Muscles, Bones, Joints and Lymph Glands

MUSCULAR DYSTROPHY (REPORT OF A FAMILY). DAVID I. ARBUSE and DAVID SLOANE, New York State J. Med. **37**:1111 (June 15) 1937.

After a review of the literature regarding muscular dystrophy Arbuse and Sloane report the history of a family in which 9 cases have occurred in three generations. In 7 cases the muscles of the shoulder girdle were involved.

AIKMAN, Rochester, N. Y.

DIFFERENT FORMS OF NON-GENERALIZED FIBROUS OSTEODYSTROPHY. E. FREUND and C. B. MEFFERT, Surg., Gynec. & Obst. **62**:541 (March) 1936.

Twenty-five cases of localized fibrous osteodystrophy are reported by Freund and Meffert. There were 18 cases of cystic and solid localized lesions, 2 of multiple localized lesions, 2 of diffuse monosseous lesions and 3 of osteodystrophia fibrosa unilateralis. The cause, the pathologic picture, the symptoms, the roentgenographic appearance and the treatment are discussed. The main object of the authors was, however, classification of the lesions according to their severity and their location. Etiologically, the factor of trauma seems to have more than accidental importance. It is also not unlikely that in a certain number of these cases there is a predisposition of the skeleton to fibrocystic osteodystrophy on an embryologic basis. In most cases the outstanding symptom is that of a fall, pain or disability in the movement of an extremity. The roentgenographic appearance is characteristically that of a cystic area or multiple cystic areas either in the metaphysis or in the diaphysis of various bones, with some sclerotic reaction around them. Localized lesions of a solid or cystic type are usually situated in the upper part of the diaphysis of the humerus, the femur and the tibia. With more extensive lesions the disease may involve the greater part of the diaphysis. Multiple localized lesions, though rare, may occur in any distribution. A unilateral form occurs with involvement of large parts, or of the entire diaphysis, of bones, arranged in longitudinal, raylike anatomic distribution. Each type of nongeneralized fibrous osteodystrophy is believed to be an abortive form of the unilateral osteodystrophy. This disease is to be differentiated from Recklinghausen's disease of the bone.

There are three methods of treatment, immobilization with a cast, the use of roentgen therapy and operative intervention. Of the three, in the hands of the author, operation and curettement of the cystic lesion of the bone gave the best results.

LAW, Ann Arbor, Mich.

THE COURSE OF SINGLE MYELOMA OF BONE: A REPORT OF 20 CASES. MAX CUTLER, FRANZ BUSCHKE and S. T. CONTRIL, Surg., Gynec. & Obst. **62**:1918 (June) 1936.

The authors report 5 cases of solitary myeloma in which the condition later became generalized. Thirteen cases are reported in which the myelomatous lesion remained localized. The lesion was still localized in 2 patients after four and ten years of observation respectively. The location of the primary myeloma varied. Only 2 of the patients with solitary myeloma had Bence Jones proteinuria. The presence of Bence Jones proteinuria supports the diagnosis of myeloma, but this symptom is not always present in the early stage of the disease.

In differentiating myeloma from giant cell tumor it must be borne in mind that the roentgenographic appearance of myeloma varies, simulating at times a giant cell tumor.

Treatment is not successful, though roentgen therapy may control the disease for a time.

LAW, Ann Arbor.

THE PROGNOSIS IN RHEUMATOID ARTHRITIS IN CHILDHOOD. THOMAS COLVER, Arch. Dis. Childhood **12**:253 (Aug.) 1937.

In an effort to determine the prognosis of chronic polyarthritis in childhood a consecutive series of 69 patients have been surveyed and follow-up inquiries pursued. The disease appears to be self limited, the average period of activity being nearly five years. In the preschool period the incidence of the disease is highest, and the mortality approaches 30 per cent. A fatal outcome is rare when the disease begins in the second half of childhood. The deaths occur in the first three years of activity. If this period is survived, the danger to life is small. Only a rough estimation of the recovery rate can be deduced. Approximately 1 in 4 patients recovers completely. Complete recovery is limited to those persons in whom the disease becomes quiescent within three years. Gross crippling is uncommon.

KELLY, Milwaukee.

EXAMINATION OF THE BONE MARROW BY STERNAL PUNCTURE. A. F. ZANATY, Lancet **2**:958 (Oct. 23) 1937.

Zanaty emphasizes the value of sternal puncture for the general study of the bone marrow in diseases of the hemopoietic system.

LANGMANN, New York.

BILATERAL CONGENITAL DISLOCATION OF THE PATELLA. MARCEL FÈVRE, Bull. Soc. de pédiat. de Paris **35**:90 (Feb.) 1937.

A girl aged 8 showed bilateral dislocation of the patella. The condition was more marked on the left, where it produced pain. Arthritis follows if the condition is not corrected. Operation on this side was decided on, and it was planned to perform a simpler operation on the other side, in which the dislocation was not causing so much pain, at a later date.

BENJAMIN, Montreal, Canada.

FRACTURE OF THE SKULL IN CHILDREN: OBSERVATIONS ON ONE HUNDRED AND NINE CASES. E. SORREL, SORREL-DEJERINE and GIGON, Bull. Soc. de pédiat. de Paris **35**:175 (March) 1937.

The case histories of 109 children admitted to the hospital with fractures of the skull during a period of four years are reviewed. A large number had no symptoms. Twenty-five showed evidence of intracranial injury. Most of the deaths occurred within forty-eight hours after the accident; only 2 children who survived the first two days died later. Of the 85 who recovered 32 were operated on. The usual observations made in cases of injury to the head were made after the children were admitted to determine whether surgical intervention was indicated; no mention is made, however, of blood pressure readings. The children were observed for long periods after their discharge from the hospital, and it was found that of 52 who were examined from six months to five years later 5.7 per cent showed sequelae which were presumed to be related to their injuries.

BENJAMIN, Montreal, Canada.

ABNORMAL ARTICULAR LAXITY. ANDRÉ TRÈVES, Bull. Soc. de pédiat. de Paris **35**:379 (June) 1937.

A boy aged 11 had abnormal laxity of all the joints of the upper extremities. This condition was not present in any other joints of the body. A roentgenogram of the left shoulder after voluntary dislocation downward so that the head of the humerus was below the glenoid cavity is shown. The boy could restore the bones to their normal position as easily as he dislocated the joints.

BENJAMIN, Montreal, Canada.

KÖHLER'S DISEASE: REPORT OF A CASE. FRANCISCO BORGES and SERGIO SANCHEN, Arch. de med. inf. **6**:463 (Oct.-Dec.) 1937.

A 5 year old child complained of pain in the foot. Roentgenograms showed the condition to be tarsal scaphoiditis (Köhler's disease). Cure was effected in three months by immobilization of the foot in inversion.

SANFORD, Chicago.

OSTEOCHONDRITIS IN AN INFANT. MARIO G. RAMOS, J. de pediat., Rio de Janeiro **4**:475 (Oct.) 1937.

The child in the case reported was 3 months old. Roentgenograms accompany the article.

SANFORD, Chicago.

DYSCHONDROSTEOSIS: REPORT OF A CASE. AQUILES GAREISO, JUAN CARLOS PELLERANO and SAMUEL SCHERE, Rev. méd. latino-am. **22**:843 (May) 1937.

The authors report a case of dyschrondrosteosis in a girl aged 7 years. The syndrome, characterized by micromelic dwarfism, was first described by Andre Leri and Jean Weill in 1929, and a short time later by Leri, Flandin and Arnandet. The cranium, the hands and the feet are normal roentgenographically. The condition is distinct from achrondroplasia and dwarfism due to rickets or syphilis. The cause is obscure. This is the first reported occurrence of the disease in childhood.

DWYER, Kansas City, Mo.

EARLY CASES OF PERTHES' DISEASE. H. GICKLER, Fortschr. a. d. Geb. d. Röntgenstrahlen **55**:441 (May) 1937.

Four cases of Perthes' disease are reported, in which the process began during the first few months of life. In no instance was physical trauma a factor of primary importance in determining the occurrence of the lesion.

MCCUNE, New York.

ENLARGED CERVICAL LYMPH NODES. LUTZ SCHALL, München. med. Wchnschr. **83**:2113 (Dec. 25) 1936.

In a lengthy article Schall discusses the differential diagnosis of enlarged cervical lymph nodes. He stresses particularly tuberculous adenopathy. Roentgen therapy is considered the best treatment for tuberculous cervical adenitis.

BRAHDY, Mount Vernon, N. Y.

THERAPY WITH GOLD COMPOUNDS IN CHRONIC ARTHRITIS IN CHILDHOOD AND THE PROBLEM OF INJURIOUS EFFECTS OF THIS TREATMENT. F. WENDEL, München. med. Wchnschr. **84**:1023 (June 25) 1937.

Although the beneficial effect of treatment with gold compounds in cases of pulmonary tuberculosis is still disputed, the results of this form of therapy in cases of chronic arthritis are excellent. They are obtained in a relatively short time. Unfortunately there may be unpleasant incidental reactions, and Wendel reports in detail their occurrence in 3 patients. One of these was a 10 year old girl who received two injections of a gold preparation three days apart. Seven days after the first injection there were noted chills, fever, adenopathy, vomiting, circulatory disturbances, cyanosis, anorexia and a morbilliform eruption. The fever subsided after three days, and in a week the child was better. Follow-up examination after three months and again after two years found the patient free from symptoms. The other 2 patients had similar reactions. The reactions occurred after small doses of a gold compound were administered. For that reason Wendel believes that these children had an unusual susceptibility to the gold compound which was used.

BRAHDY, Mount Vernon, N. Y.

THE LATE RESULTS OF OSTEOMYELITIS OF THE LOWER ARM. J. BERNER, Röntgenpraxis **9**:418 (June) 1937.

The case of a 65 year old man is reported. It illustrates the severity of deformity which may result from osteomyelitis in infancy.

McCUNE, New York.

OSTEOGENESIS IMPERFECTA CONGENITA: REPORT OF FIVE CASES. M. HAYAKAWA, Acta pædiat. japon. **43**:1163 (Aug.) 1937.

Sixty-seven cases of this disease are reported in the Japanese literature. The author adds reports of 5 cases; the patients were first seen at the ages of 14 days, 19 days, 1 month, 5 months and 7 months, respectively. In all cases the clinical manifestations were identical: softness of the cranium, shortening and deformities of the extremities and abnormal fragility of the bones. Characteristic roentgenograms of the bones are described. In only 1 instance was a familial tendency noted; the first sibling of this family died from the same anomaly soon after birth.

KATO, Chicago.

THE SYNDROMES OF STILL, CHAUFFARD-RAMOND AND FELTY. T. F. BLOEM, S. VAN CREVELD, F. C. KUIPERS and P. J. ZUIDEMA, Nederl. tijdschr. v. geneesk. **81**: 5601 (Nov. 20) 1937.

A survey of the clinical features of the syndromes of Still, Chauffard-Ramond and Felty is presented. Stress is laid on the fact that all these diseases up to the present time are considered separate clinical entities and therefore should not be considered as different forms of one disease. The effect of therapeutic measures is dealt with, special attention being drawn to splenectomy, which was performed on 2 patients, 1 adult and 1 girl. The girl had suffered since the age of 8 years from a severe form of Still's disease, and as all therapeutic measures had failed splenectomy was performed when she was 14 years old. There were immediate relief of the pains and great amelioration of the condition. However, after one year another attack of the disease occurred.

VAN CREVELD, Amsterdam, Netherlands.

Skin Diseases; Allergy

XERODERMA PIGMENTOSUM WITH CARCINOMA OF THE LOWER LIP IN TWO BROTHERS, AGED SIXTEEN AND THIRTEEN YEARS. E. T. BELL and T. P. ROTHNEM, Am. J. Cancer **30**:574 (July) 1937.

Two brothers, aged 16 and 13 years, exhibited early lesions of xeroderma pigmentosum, and squamous cell epithelioma of the lower lip developed in each. The diagnosis of epithelioma in each case was confirmed by histologic examination, and each lesion healed after intensive roentgen therapy of the lip and the regional glands. The father and the mother, aged 52 and 40 years, respectively, were second cousins and of Swedish descent.

FOERSTER, Milwaukee. [ARCH. DERMAT. & SYPH.]

AN EARLY SIGN OF LATENT ALLERGY IN INFANTS. I. NEWTON KUGELMASS, Arch. Dermat. & Syph. **36**:343 (Aug.) 1937.

The author states: "The difficulty of recognizing allergy early is greatest in the case of infants, as in infancy ill defined conditions are usually atypical in their manifestation." A hairless, scaly scalp or a desquamated dry skin is a helpful sign in the recognition of allergy in infants. Retroauricular intertrigo is a fairly constant concomitant of latent allergy. It is best seen when the ear is pulled forward.

DULIN, Iowa City.

CEREBRIFORM NEVUS RESEMBLING CUTIS VERTICIS GYRATA. G. HAMMOND and H. K. RANSOM, Arch. Surg. **35**:309 (Aug.) 1937.

Cutis verticis gyrata is a disease of the scalp characterized by the presence of a variable number of convolutions, or gyri, separated by furrows, or sulci. Two cases of this rare condition are described, and the several theories dealing with the causes and the nature of the nevus are discussed. The treatment, the authors point out, is surgical and consists in either complete excision with subsequent grafting of skin or gradual partial excision with closure.

KAISER, Rochester, N. Y.

RELATION BETWEEN "SYSTEMIC" LUPUS ERYTHEMATOSUS AND A PECULIAR FORM OF THROMBOCYTOPENIC PURPURA. HARRY KEIL, Brit. J. Dermat. **49**:221 (May) 1937.

In this case the first clinical manifestation was thrombopenic purpura, which was apparently cured by splenectomy. Ten months later signs of systemic lupus erythematosus appeared. The patient eventually died of renal insufficiency due to residual alterations in the kidneys (so-called hyaline thrombi). Thrombopenic purpura is usually explained on the basis of overactivity of the spleen or diminished function of the bone marrow. It is probable that there is in some cases, as apparently there is in this one, a third mechanism: withdrawal of platelets from the general circulation by their inclusion in capillary thrombi distributed throughout the body. Keil, from similar cases in the literature, cites evidence indicating a relation between systemic lupus erythematosus and this variety of thrombopenic purpura. He discusses in general the relation of the two diseases to vascular disease of the small vessels, the formation of so-called hyaline thrombi, the tendency to purpura in lupus erythematosus and the factor of therapy with gold preparations in the production of purpura. The pertinent literature is reviewed.

RATTNER, Chicago. [ARCH. DERMAT. & SYPH.]

THE MECHANISM OF HERPES ZOSTER AND ITS RELATION TO CHICKENPOX. E. S. STERN, Brit. J. Dermat. **49**:263 (June) 1937.

Stern concludes from his study of 31 cases that the eruption of herpes zoster is caused by infection passing from the sensory ganglion down the course of the sensory nerve to the skin. The extension of the eruption in a case of zoster was not prevented by blocking an involved sensory nerve with alcohol. The eruption usually spreads in a distal direction along the distribution of the sensory nerve. It is usually more intense proximally. The sensory nerve was found to be the seat of hemorrhage and inflammation in a case of ophthalmic zoster. Of the 31 subjects, 4 caused varicella in persons with whom they came in contact.

RATTNER, Chicago. [ARCH. DERMAT. & SYPH.]

FETAL ICHTHYOSIS IN A DOG. A. HENRY and L. BORY, Bull. Soc. franç. de dermat. et syph. **44**:325 (Feb.) 1937.

The authors state that the more that dermatoses of animal and man are compared the more does one find likenesses. They report the case of a 7 month old pup with fetal ichthyosis. The skin was thickened, scaly and without hair over the affected parts. The eruption, which was of linear distribution, involved the front feet and progressed up the sides of the chest. Until the age of 6 months the general health of the animal remained normal. Shortly thereafter the dog had a convulsion, atony of the sphincters and excessive salivation. A similar though shorter crisis occurred five days later.

The authors discuss true and congenital ichthyosis in human beings. True ichthyosis has never been observed to appear in animals after birth. The severe type of fetal ichthyosis (with lesions present at birth) has been noted in animals, almost exclusively in calves. This type of dystrophy, just as in the human being, is incompatible with life.

The benign type of fetal ichthyosis corresponds to Brocq's congenital ichthyosiform erythroderma, and the authors classify the condition in the case in question in that category. LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

PEMPHIGUS WITH EPIDERMAL CYSTS AND ALBOPAPULOID FORMATIONS. H. CERRUTI and J. DA FONSECA BICUDO JR., Arch. de dermat. e syph. de São Paulo **1**:9 (March) 1937.

The authors report the case of a boy of 16 years who had typical dystrophic epidermolysis bullosa hereditaria. A maternal aunt and uncle are said to have a similar but less marked condition; the parents are not consanguineous. The eruption began several years after birth and at the time of examination involved chiefly the feet, the knees, the hands, the elbows and to a lesser extent the trunk. There were serous and hemorrhagic bullae, cicatrized atrophic areas, myriads of white grainlike epidermic cysts and dystrophic changes in the nails. Over the lower part of the back the skin was wrinkled like crepe paper and atrophic, giving the impression of papular elevations (albopapuloid formations). The Nikolsky sign was not present except in the atrophic areas. The histologic studies showed edema of the epidermis and dermis, intraepidermal and dermoepidermal bullae, areas of atrophy and epidermal cysts, which at times involved the sweat ducts and the pilosebaceous follicles. A consistent decrease to absence of elastic fibers was evident under the orcein stain in the upper layers of the corium; their amount was normal in the deeper layers. Extensive laboratory studies were made, including tests for hemoporphyrinuria, but no abnormality was discovered. It is noteworthy that while the patient was under observation rheumatic fever developed, with evidences of mitral stenosis and pericardial effusion.

LEIFER, New York. [ARCH. DERMAT. & SYPH.]

XERODERMA PIGMENTOSA IN AN EIGHT YEAR OLD GIRL. J. ZIENKIEWICZ, Pedjatrja polska **17**:107 (March-April) 1937.

For nine months the child showed red patches on the skin, pallor, malnutrition, loss of weight, photophobia, tearing of the eyes, eversion of the lower eyelids and finally multiple tumors on the skin with ichthyotic change. The diagnosis was difficult. The tuberculin and Wassermann tests were negative. This condition is rare. Fifty-one per cent of the cases have occurred in children of parents who have intermarried with close relatives. Occasionally syphilis may cause this condition. The treatment is palliative, with use of a high vitamin diet and roentgen rays. The response is slow.

KRUPINSKI, Chicago.

SEPSIS CAUSED BY MULTIPLE ABSCESSES OF SWEAT GLANDS IN A BABY. J. RUDING, Nederl. tijdschr. v. geneesk. **81**:4959 (Oct. 16) 1937.

A case of pyoderma in a baby aged 4 weeks is described. The staphylococcic infection, which had caused nodules, abscesses and ulcers, had probably originated in the region of the sweat glands, though this hypothesis could not be proved histologically. Sepsis arose, causing the death of the baby at the age of 4 months. In the beginning of the disease a diagnosis of pyema with hematogenic changes of the skin had been made.

VAN CREVELD, Amsterdam, Netherlands.

THE ETIOLOGY OF ECZEMA. K. EDEL, Nederl. tijdschr. v. geneesk. **81**:6006 (Dec. 18) 1937.

From the results of his own investigations and those of others, the author concludes that the theory that allergy is the cause of eczema is incorrect and that the cause may be parasitic. The forms of eczema occurring in children and showing a certain degree of clinical deviation from those observed in adults do not, in the author's opinion, arise from a different cause. The differences are principally

caused by the peculiar sensitivity of the nervous system in childhood, which gives rise to a severe and long-lasting allergic reaction toward cocci and their toxins. The author believes that it is logical to employ remedies of an antiparasitic nature, such as sulfur and salicylic acid.

VAN CREVELD, Amsterdam, Netherlands.

Miscellaneous

STUDIES ON THE ALLEGED TOXIC ACTION OF COD LIVER OIL. ETHEL BURACK and H. M. TIMMERMAN, J. Nutrition **14**:535 (Dec.) 1937.

Rats and mice were given diets containing a high percentage of cod liver oil. The cod liver oil supplied the dietary fat. Among control groups oil of peanut supplied the dietary fat.

Animals were killed at various periods in the course of the experiments, and histologic examinations were made of the heart, the liver, the kidney and the skeletal muscles. Some pathologic changes in these structures were found in a few animals. However, changes in the organs were found in such small a percentage of the animals that the authors were unable to substantiate the claim that cod liver oil in therapeutic doses can exert injurious effects.

MUNNS, Winnetka, Ill.

FEVER THERAPY IN CHILDREN. LOUIS SPEKTER and ANGUS MCBRYDE, J. Pediat. **11**:499 (Oct.) 1937.

The literature on artificial fever therapy is reviewed, and a report on 32 children treated by means of radiant energy is presented. The risks of fever therapy and the physiologic reactions to fever are discussed. The method used and the radiant energy cabinet are described. The treatment was most successful with gonorrheal infections. In the cases of chronic infectious arthritis immediate improvement followed treatment, but subsequent relapse was the usual course. Among the syphilitic patients treated, 1 child with juvenile paresis showed definite improvement after the second series of arsphenamine and fever therapy. Another child, suffering from interstitial keratitis, was given two treatments which caused much of the exudate in the anterior chambers and the corneal opacities to disappear, but six months later the patient, having received no specific therapy in the interim, could barely distinguish large objects. Eight patients with chorea were treated by this method, and the results compared favorably with those obtained with the intravenous injections of typhoid-paratyphoid vaccine. The authors believe that the latter method is to be preferred in the treatment of chorea because it is easier to give and the results are as good as those obtained with controlled fever. The authors conclude that artificial fever treatment is of value in certain diseases but is still in the experimental stage.

RAUH, Cincinnati.

PHLEBOCLYSIS AND DEHYDRATION IN INFANTS. J. COMBY, Bull. Soc. de pédiat. de Paris **35**:21 (Jan.) 1937.

Phleboclysis is considered a better term than venoclysis. The early results of this treatment are good, and further results are awaited before a definite opinion is expressed.

BENJAMIN, Montreal, Canada.

THE HISTORY AND ACTUAL STATE OF PEDIATRICS IN POLAND. M. MICHALOWICZ, Bull. Soc. de pédiat. de Paris **35**:317 (June) 1937.

The first Polish book dealing with diseases of children was published in Latin by Chrosciejewski in 1583. The beginning of modern pediatrics in Poland dates from 1805, when a medical school was founded in Vilna. In 1833 a pediatric service of twelve beds was begun in Cracow. In 1864 the first chair of pediatrics was founded in Poland; it was first occupied by Jakubowski. In 1903 another center of pediatrics was established at Lodz, with Brudzinski in charge. In 1908 the first issue of *Przeglad pedyatryczny* appeared. At present there are 5 pediatric

clinics and 12 hospitals for children and also a number of pediatric services in general hospitals, making a total of 3,573 beds for sick children in Poland. There is a Polish pediatric society which conducts a pediatric congress every four years. A bibliography of over 8,000 Polish pediatric publications has been collected to date.

BENJAMIN, Montreal, Canada.

HEREDITARY TRANSMISSION OF M AND N. E. PONZI, Riv. ital. di ginec. **19**:462, 1936.

Ponzi determined the MN types of 100 pairs of parents and their children and did not encounter a single exception to the theory of heredity of Lansteiner and Levine.

A. S. WIENER. [ARCH. PATH.]

SOME CASES IN A PEDIATRIC PRACTICE. R. A. SCATENA, Rev. Soc. de pediat. de Rosario **2**:137 (Sept.) 1937.

A case of leukemia in which radiotherapy was used, vulviform hypospadias and the treatment of constipation in infancy are discussed.

SANFORD, Chicago.

THE TREATMENT OF SEPTIC AND SIMILAR CONDITIONS WITH DERIVATIVES OF SULFANILAMIDE. JOHANN SCHMIDT, München. med. Wchnschr. **83**:2122 (Dec. 25) 1936.

Schmidt reports good results in cases of erysipelas, follicular tonsillitis, septic abortion and typhoid with the use of derivatives of sulfanilamide.

BRAHDY, Mount Vernon, N. Y.

FOOD POISONING BY STAPHYLOCOCCI. W. A. TIMMERMAN, Nederl. tijdschr. v. geneesk. **81**:4443 (Sept. 18) 1937.

A small outbreak of food poisoning (of 1 adult and 2 children) which resulted from the ingestion of pork liver sausage is reported. From the incriminated sausage staphylococci could be recovered which were capable of generating in broth an enterotoxic substance which when taken by mouth produced unmistakable symptoms of food poisoning in a human volunteer. Staphylococcic food poisoning (for example, after consumption of cheese) is probably more prevalent in the Netherlands than was formerly supposed.

VAN CREVELD, Amsterdam, Netherlands.

THE RESULTS OF TREATMENT WITH AUTOGENOUS VACCINES. J. B. WOLFF, Nederl. tijdschr. v. geneesk. **81**:5106 (Oct. 23) 1937.

An analysis is given of the result of treating different chronic bacterial infections with autogenous vaccines. Excellent results were seen in cases of furunculosis, angina chronica (most of the patients being children) and chronic otitis (Bacillus pyocyaneus). These were less constant in cases of cystitis and of pyelitis, although in some of these cases the condition responded only to treatment with autogenous vaccines. This treatment gave some improvement in 1 or 2 cases of pyorrhea alveolaris, but on the whole the results with this infection were unsatisfactory. In the treatment of chronic angina and of otitis due to B. pyocyaneus polyvalent stock vaccines in some cases showed the same therapeutic values as autogenous vaccines.

VAN CREVELD, Amsterdam, Netherlands.

THE TREATMENT OF SMALL BURNS. J. W. LOOS, Nederl. tijdschr. v. geneesk. **81**:5674 (Nov. 27) 1937.

The treatment of small burns is found to be favorably influenced by the use of a 2 per cent solution of mercurochrome, which sterilizes the surface of the wound without damage to the cells.

VAN CREVELD, AMSTERDAM, Netherlands.

Society Transactions

SOCIETY FOR PEDIATRIC RESEARCH

SAMUEL Z. LEVINE, M.D., *President, in the Chair*

Annual Meeting, Great Barrington, Mass., May 4 and 5, 1938

A. A. WEECH, M.D., *Secretary*

First Session

Wednesday Afternoon, May 4

VITAMIN C DURING LACTATION. DR. T. INGALLS, MISS RUTH DRAPER and MR. H. TEEL, Boston.

This paper will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

DIABETES, CARBOHYDRATE COMBUSTION AND INSULIN ACTION. DR. E. M. BRIDGE and MISS ELEANOR A. WINTER, Baltimore.

The view is commonly held among clinicians that insulin acts as a specific hormone which makes possible the combustion of carbohydrates and that variations in the blood sugar level of diabetic patients reflect the intensity of the insulin effect. A study of the blood sugar levels and of the respiratory quotients of diabetic children throughout the day has shown that (1) hypoglycemia is associated not with evidences of stimulated carbohydrate combustion but with constant or decreasing respiratory quotients at average normal levels; (2) hyperglycemia may also develop in the presence of a constant respiratory quotient at a normal level. The results cannot be correlated with the usual conception of the physiology of diabetes and the action of insulin.

Since the principal effect of an overdose of insulin in animals is to force the deposition of glycogen in the muscles instead of in the liver, insulin hypoglycemia in all probability is a result of this action, not of excessive combustion. The variations in the respiratory quotient observed in the study can be correlated with expected changes in hepatic glycogen, a relationship recently demonstrated in animals.

Since the blood sugar level is not an accurate guide to the entire disturbance in the carbohydrate metabolism of diabetes, it is suggested that other criteria should be given more attention.

ABSORPTION OF DEXTROSE FROM THE SMALL INTESTINE IN INFANTS AND CHILDREN. DR. ALICE D. CHENOWETH, Philadelphia.

The absorption of dextrose, galactose and levulose from the upper part of the small intestine in infants and children convalescing from diseases other than gastrointestinal was studied by means of the intubation method devised by Miller and Abbott (1934). The specially constructed tube had a double-lumen (no. 14 French, Miller II) and was 1 meter long. At the distal end was a collapsible balloon, which acted as a barrier to the passage of intestinal contents. One lumen controlled this balloon; a second communicated through a series of perforations with the lumen of the intestine.

The tube was passed in the routine manner into the stomach, with the subject on his right side; it was advanced slowly until its tip was in the duodenum. Here the balloon was inflated to promote the more rapid advance of the tube into the upper part of the jejunum, where the position was identified fluoroscopically. Thus the upper part of the intestinal tract, consisting of duodenum and upper jejunum, was blocked off, and the absorption of sugars from this area was tested.

In the older children, 100 cc. each of a 5, a 7.5 and a 10 per cent solution of dextrose and of a 5 and a 7.5 per cent solution of galactose and of levulose were introduced for two successive periods of thirty minutes each. The solution remaining at the end of each period was withdrawn, and its sugar content was determined. The intestine was washed at the end of each period, and the amount of sugar in the washings was also measured. In the experiments in which infants were used, 50 cc. of a 5 per cent solution of dextrose was introduced for varying periods. Determinations of sugar content were made by Benedict's colorimetric method.

The results were as follows:

1. In the concentrations tested, increased absorption occurred with increasing concentrations of sugar.

2. The quantity of sugar absorbed was proportional to the time allowed for absorption.

3. The percentage of sugar withdrawn after a thirty-minute period of absorption tended to be rather constant (2 to 3 per cent), regardless of the strength of the solution introduced.

4. Greater volumes were withdrawn when higher concentrations of sugars were used.

5. There was less absorption of sugar during the second periods than during the first.

6. No relation between rate of absorption and body weight was found.

7. Dextrose and galactose appeared to be absorbed at approximately the same rate, whereas levulose was absorbed at a somewhat lower rate.

8. The amounts of sugar used were too small to be registered in rises in the blood sugar level.

HEPATIC INSUFFICIENCY AS A CAUSE OF MALNUTRITION IN INFANTS. DR. S. LIVINGSTON, Baltimore.

Oral dextrose tolerance tests in infants have been used often as an aid in the diagnosis of celiac disease, a flat blood sugar curve being usual with this condition. Relatively little attention, however, has been given to the importance of the amount of dextrose given or to the length of the period of fasting which precedes the test.

The present work began as an attempt to standardize the dextrose tolerance test in infants. Essentially normal convalescent babies in the hospital wards were used as subjects. After a standard fasting period of twelve hours, they were given 1, 1.75 or 3 Gm. of dextrose per kilogram of weight, and the blood sugar level was tested at the usual intervals. The average value during fasting for the group given 1 Gm. per kilogram was 82 mg. per hundred cubic centimeters with a peak of 116 mg. in one hour; for the group given 1.75 Gm. per kilogram, 84 mg. with a peak of 133 mg. in one hour, and for the group given 3 Gm. per kilogram, 82 mg. with a peak of 171 mg. in one hour. I believe that 3 Gm. of dextrose per kilogram of weight given after a twelve hour period of fasting constitutes the most satisfactory standard for the dextrose tolerance test for infants.

Some time after the study was begun, the largest dose of dextrose was administered to 2 infants whose only difficulty was failure to gain weight with a supposedly adequate formula.

The first patient was a 2 month old infant with congenital syphilis. After the first and only injection of sulfarsphenamine she had a severe reaction. Recovery followed in one week, but for two months thereafter the liver remained large and she failed to gain weight in spite of a feeding (usual proportions of carbohydrate, fat and protein) of 200 calories per kilogram which she took hungrily.

The second patient was a 6 week old premature girl admitted to the hospital with nonspecific diarrhea. After ten days the diarrhea cleared up, but for the following month the patient failed to gain weight in spite of the fact that her feedings (usual proportions of carbohydrate, fat and protein) were increased to 280 calories per kilogram. She took her feedings hungrily. The liver was not enlarged.

Low dextrose tolerance curves with hypoglycemic values during fasting were found in both cases. Levulose tolerance tests also gave abnormal results. The feedings of both patients were increased in such a way as to keep constant the total calories and the protein intake, the essential change being a substitution of dextrose for half of the fat. Both patients responded almost immediately with a dramatic gain in weight. The effect on general appearance and activity was equally remarkable. The enlarged liver receded to normal size. After improvement the blood sugar values during fasting and during tolerance tests returned to normal.

I believe from the data that insufficiency of the liver accounted for the disturbance and was responsible for the malnutrition in both cases.

LONGITUDINAL AND CROSS-SECTIONAL DATA ON STORAGE OF NITROGEN AND CALCIUM IN ACTIVELY GROWING CHILDREN. DR. ICIE G. MACY, Detroit.

Twenty-one children between the ages of 4 and 10 years were observed under continuous metabolic regimens varying from two to thirty-two weeks in length, and the same children were observed at different age levels. This permitted practical consideration of the conventional types of interpretation of metabolic data in comparison with newer and more significant methods. Storage of nitrogen and calcium was observed by means of longitudinal and cross-sectional study of subjects under a given environmental and dietary regimen. The study included cumulative and average daily storage of calcium; the analogy of skeletal maturity to storage of calcium; adjustment or preparation for metabolic studies; gain or loss in body weight versus storage of nitrogen, and longitudinal storage of nitrogen and calcium in relation to dietary intake, in the growing child as compared with the adult.

TOTAL AND DIFFERENTIAL COUNTS, RATE OF DISINTEGRATION AND LIPID COMPOSITION OF PLATELETS. DR. PEARL LEE and MISS BETTY N. ERICKSON, Detroit.

Interrelated studies on human blood platelets were undertaken with the view of obtaining information on their role in blood clotting in health and in disease. These studies consisted of total and differential counts, determinations of disintegration rates and detailed lipid analyses made on platelet preparations.

Observations were made on 10 normal women, 4 of whom were studied during menstruation, 4 normal men and 10 hemophilic children.

The technic of Olef for total and differential platelet counting was chosen for these studies (*J. Lab. & Clin. Med.* **22**:129 [Nov.] 1936). The method consists of collecting blood obtained by finger puncture in a paraffin cup, using a solution of sodium metaphosphate to prevent clumping. Counts are made from a fresh preparation of this mixture. The platelets are differentiated into three classes according to size, the red cell being used as a standard. Group I is one-quarter the size of the red cell, group II one-third and group III one-half.

About 75 per cent of both the normal and the hemophilic subjects had total counts ranging between 600,000 and 800,000. The lowest was 350,000 and the highest 1,000,000.

Normal differential counts showed that group I remained fairly constant, while a variation in group II explained the differences in the total counts.

Hemophiliacs gave a moderately higher percentage of group I than the normal subjects. Studies of the disintegration rate of the normal subjects gave in general a 20 to 40 per cent reduction in the total count after the material had been in the incubator six hours. Group II was usually definitely reduced, while group I remained approximately the same or was increased. However, the hemophiliacs showed no decrease in the total count and a different type of change in the differential. Group II was increased by 25 to 50 per cent, while group I was decreased.

The menstruating women had platelet counts strikingly similar to those of the hemophilic children. Here the disintegration rate was retarded, the retardation beginning from one to four days before the onset of menstruation. The differential count at the end of six hours varied somewhat but usually indicated the type of distribution found for the hemophilic patients.

Clotting time during menstruation was definitely prolonged, ranging from fifteen to twenty minutes. Between the periods it was ten to twelve minutes.

In Brich's work on hemophilia, she advanced the theory that the female carrier is protected from bleeding by her "sex hormones." The findings here might suggest that endocrine changes produce a type of bleeding during menstruation which is similar in some respects to that of hemophilia.

Detailed lipid analyses of platelets of normal adults and children showed a composition similar to that of human erythrocyte stroma. The values were slightly lower for children than for adults. Platelets from three groups of hemophilic subjects gave essentially the same values as platelets from the normal children for phospholipid, neutral fat and cholesterol. Perhaps the slow disintegration rate was due to abnormalities of the plasma rather than to deficiencies of the platelets themselves.

FIBRINOLYTIC TEST AS A DIAGNOSTIC AID. DR. P. L. BOISVERT, New Haven, Conn.

The streptococcic fibrinolytic test of Tillett and Garner had promise of being a practical serologic test for recent hemolytic streptococcic infection. However, the test has subsequently been reported as nonspecific and therefore of little diagnostic value.

In the pediatric clinic, early use of the test corroborated the reports of its nonspecificity. It seemed of much interest, however, to study the behavior of the test in the course of nonstreptococcic diseases and of diseases caused by the hemolytic streptococcus. This report represents a study of the trend of the fibrinolytic test for 15 normal persons of the pediatric age group and for 206 patients with various types of infection.

Five types of trend were observed: (1) early positive results of the tests (resistant clot) becoming negative (rapidly lysed clot) during convalescence; (2) early negative changing to positive with recovery; (3) persistently positive; (4) persistently negative, and (5) positive changing to negative and later becoming positive again.

These types were associated with the following conditions:

Type 1 was frequently observed with the more severe nonstreptococcic infections and occasionally with a hemolytic streptococcic illness.

Type 2 occurred with most hemolytic streptococcic diseases and was not seen with other conditions.

Type 3 was found with rheumatic fever and acute hemorrhagic nephritis and in some cases of hemolytic streptococcic infection.

Type 4 was universally present in tests for normal children, with most mild infections and with some infections due to the hemolytic streptococcus (mainly in infants or in older children with complications).

Type 5 appeared when nonstreptococcic infections were followed during convalescence by a streptococcic illness.

This study suggests that the fibrinolytic test may be of diagnostic aid. Although a single test may be of no value unless viewed in the light of the history and the bacteriologic findings, the trend of several tests may be significant. The type of trend that was observed in tests for the majority of patients with hemolytic streptococcic infection was found with no other type of disease.

DIAGNOSIS OF CONGENITAL MALFORMATIONS OF THE HEART IN INFANTS WITH PERSISTENT CYANOSIS. DR. HELEN B. TAUSSIG, Baltimore.

The method is based on the fact that many malformations are associated with gross defects in the heart and with malformations of the great vessels. A number of them cause sufficient alteration in the size and shape of the heart and vessels to be recognized by fluoroscopic examination. Fluoroscopic study of the heart in the left and right oblique positions as well as in the anteroposterior view permits differentiation of each of the four chambers of the heart and of the great vessels. Therefore, enlargement or absence of these chambers can be recognized.

To interpret the outline of the malformed heart, it is essential to understand the contour of the normal heart. The infant's heart occupies a more transverse position in the thorax than does the adult's. The left border of the cardiac silhouette is composed of the pulmonary conus of the right ventricle and the left ventricle. The tip of the left auricle is not visible. The shadow to the right of the sternum is cast by the right auricle. The left anterior oblique position permits differentiation between the two ventricles. The anterior part of the shadow is formed by the right ventricle and the posterior part by the left ventricle. The size of the right ventricle is estimated by its relation to the aorta and the size of the left ventricle by the amount of rotation necessary for the heart to clear the spinal column. The left auricle is normally not clearly visualized.

Alterations in each of the chambers cause a specific change in the shape of the heart. Enlargement of the right ventricle is usually associated with accentuation of the shadow cast by the pulmonary conus; it can always be recognized in the left antero-occipital position by the extension of the cardiac shadow anterior to the aorta. Absence of the right ventricle causes absence of the pulmonary conus and in the left antero-occipital position absence of enlargement anterior to the aorta. Left ventricular enlargement is best recognized in the left antero-occipital position by an increase in the rotation necessary for the heart to clear the vertebral column. Enlargement of the right auricle is seen in the anteroposterior view by an extension of the cardiac shadow to the right of the sternum. Enlargement of the left auricle is detected in the right antero-occipital position by backward displacement of the esophagus filled with barium sulfate.

Abnormalities in the great vessels can be studied similarly. A limited number of variations is possible: diminution in size or atresia of the pulmonary artery or of the aorta, complete or partial transposition of the great vessels or a single truncus arteriosus. Under the fluoroscope, each has characteristic features.

With the information obtained by fluoroscopic study and by the various peripheral manifestations, such as the strength of the pulse in arm and leg, the distribution of the cyanosis and pulsation in the liver or lungs, the nature of the malformation is determined.

By this method I have learned to recognize a nonfunctioning right ventricle, transposition of the great vessels, complete interruption of the isthmus of the aorta with or without transposition, a single ventricle with a primitive outlet chamber, and a single truncus arteriosus.

THE BIOPHOTOMETER (FROBER-FAYBOR) IN TESTING VITAMIN A DEFICIENCY. DR. C. E. SNELLING, Toronto, Canada.

A group of average Toronto school children were tested for dark adaptation with the biophotometer on repeated occasions during the past year. The instrument was similar to that described by Jeans, Blanchard and Zentmire, and the technic and standards reported by them were used. The first test was repeated

within three weeks with no addition to the diet. The children were then given 13,000 units of vitamin A in the form of 50 per cent percomorph liver oil daily for three weeks, and a third test was made. The oil was continued for a second three week period, and a fourth test was made. The results obtained were obviously variable, showing no consistency, and there was no evidence of improvement as a result of vitamin A. In conclusion, I have found the biophotometer unsatisfactory as a method of estimating the variations in dark adaptation which might be produced in children by vitamin A deficiency.

PHYSICAL AND MENTAL DEVELOPMENT OF CHILDREN WHO LATER BECAME PSYCHOTIC. DR. G. E. GARDNER, Boston.

Few data exist on the physical and mental development of children who later become insane or show marked emotional instability.

In 1922 the Harvard University Graduate School of Education began a twelve year study of 3,200 school children, on whom physical and mental measurements were taken annually. Of this group, 22 had been admitted to a psychopathic hospital by the time they had reached the twentieth year. In 8 cases the condition was definitely diagnosed as psychotic, the disorder in 1 being juvenile dementia paralytica.

A survey of the physical growth of these 22 patients in childhood reveals that (1) their physical development was not retarded or accelerated, (2) they were not preponderantly of any particular body type and (3) there was no deviation from normal in the physical development of those whose mental illness began during this twelve year study.

A summary of the mental development of the 22 patients during childhood shows that (1) there were no definitely feebleminded children in the group, (2) none of them attained a rating of superior intelligence and (3) with the exception of the patient with paralytic dementia, who showed a marked diminution in his intelligence quotient before hospitalization, successive tests of the intelligence quotients revealed no variations great enough to warrant a change from the diagnostic group into which the subjects fell at the time of their initial examination, at 5½ to 6 years of age.

I conclude that these patients had essentially normal physical and mental development in childhood. The patient with juvenile paralytic dementia was an exception to these findings in that he began to show marked physical and mental retardation four years before hospitalization.

GROWTH FACTOR IN OBESE CHILDREN. DR. HILDE BRUCH and DR. R. L. DAY, New York.

This report deals with observations on 80 obese children 2½ to 13 years old. Excessive weight was the outstanding clinical symptom; in terms of the Baldwin-Wood standards they were from 25 to 100 per cent overweight. By comparing the height of these obese children with the average normal height in the charts prepared by Burgess it could be demonstrated that obese boys and girls are markedly advanced in growth in stature.

Skeletal maturation was advanced also. Roentgenograms of the hands of 50 obese children were rated according to the standards of Todd and of Flory. Thirty-six children showed advanced skeletal age, 12 were within the zone of average normal growth, and only 2 exhibited some retardation.

Among the 40 girls, 19 were between the ages of 9 and 13 years; 8 of them were menstruating, 4 having commenced to menstruate between the ages of 9 and 10 years; in 9, secondary sex characteristics were well developed; only 2 failed to show signs of beginning puberty. The average age of onset of puberty was given by Engle as 13½ years. Our observations suggest that puberty occurs early in obese girls.

Among the boys, 10 were 11 to 13 years old; 6 of them showed signs of approaching puberty. Such data do not suggest any delay in sexual development.

The circumstances brought out in this study are in harmony with observations made on 3,600 normal boys and girls in the Laboratory School in Chicago. Longitudinal records of height and weight from the age of 6 to the age of 17 years were arranged with respect to age at the onset of puberty. Height and weight were greater in the groups who matured early, the difference in weight throughout the period of growth being more marked than the superiority in height.

It may be concluded that the findings for obese children merely show exaggeration of a trend observed in the normally nourished. On the other hand, the observations are directly opposed to those theories which attempt to explain obesity on the basis of hypothyroidism or hypopituitarism.

Second Session

Thursday Morning, May 5

ASSAY OF FOODS FOR POTENCY IN PROMOTING FORMATION OF SERUM ALBUMIN. DR. A. A. WEECH and DR. ELVIRA GOETTSCH, New York.

A method is described for assaying food proteins with respect to their potency in promoting the formation of serum albumin. Depletion of serum albumin is induced in dogs by feeding a basal diet low in protein. The diet is supplemented by adding the test food, and the rise in albumin concentration during a standard period of one week is measured. When the concentrations are expressed in grams per hundred cubic centimeters of serum, the assay value is calculated as the concentration increment plus 0.15. The added constant represents in grams per hundred cubic centimeters the average decrement in concentration during the same period with the basal diet when no test food is added; it embodies in the assay value an allowance for maintenance. The potency value of a test food is the average of a number of assay values derived from experiments with different animals.

The potency values of 6 test foods as determined by this method of assay are as follows: beef serum (11 animals), 0.8; egg white (3 animals), 0.67; beef liver (5 animals), 0.48; beef muscle (12 animals), 0.48; casein (12 animals). 0.39, and gelatin (4 animals), — 0.09. Statistical analysis shows that beef serum is significantly more potent than beef liver, beef muscle, casein or gelatin. Gelatin is significantly less potent than any of the other foods.

PRECIPITIN STUDIES FOR PATIENTS WITH DISEASES OF THE KIDNEY. DR ELVIRA GOETTSCH and DR. J. D. LYTTLE, New York.

Precipitin studies were carried out on the serums of 21 patients with nephrosis and of 17 patients with nephritis. An arbitrary level of 40 per cent deficit between the values obtained by Howe's method and those obtained by the precipitin method will effectively distinguish the nephrotic from the nephritic patient during the acute stage of the disease. In most of the nephrotic patients the albumin deficits were over 40 per cent, with or without an accompanying globulin deficit; in most of the nephritic patients the albumin deficit was under 40 per cent, with no accompanying globulin deficit.

Since the deficits disappeared during convalescence, it was assumed that both nephrotic albumin and nephrotic globulin are mixtures of some normal serum protein and a changed protein with altered serologic reactions. Antiserums were produced against nephrotic albumin and against nephrotic globulin; the antibodies to the normal serum protein were absorbed out, leaving antiserums which theoretically contained antibodies to the changed protein only. With these absorbed antiserums results were obtained which suggest that the changed nephrotic albumin does not stimulate formation of antibody in the rabbit but that the changed nephrotic globulin is antigenic in character. The absorbed nephrotic globulin antiserums reacted with the serums of patients in the edematous stage of nephrosis but not with serums from normal human beings or with those from patients cured of nephrosis.

Significance of Conditions of Exposure in the Study of Prophylaxis Against Measles. Dr. S. Karelitz, New York.

The results in 583 children exposed to measles and treated prophylactically were analyzed to evaluate the importance of the type or the conditions of exposure. As reported in previous work published with Dr. Schick, there were great differences in the rate of secondary attack, which depended on whether or not the exposure took place in hospital wards or in homes with different hygienic conditions.

The study was extended to include exposure to measles presumably acquired in school rooms, play groups, at parties and in public vehicles. The results indicate that there is a very low incidence of measles among the children exposed under such conditions. This circumstance often leads to the false impression that the prophylactic substance used was successful and explains a great deal of the discrepancy in the results reported in the literature by various persons using similar preparations in prophylaxis against measles. The data show the necessity for considering type of exposure in the evaluation of any substance prophylactic against measles. They also indicate that measles is transmitted primarily by direct contact and that the dose of infection with measles determines to a considerable degree what the rate of secondary attack will be.

Changes in the Organic Acid-Soluble Phosphorus of Blood Cells (Especially the Diphosphoglyceric Acid Fraction) in Different Pathologic Conditions: Clinical and Experimental Studies. Dr. G. M. Guest and Mr. S. Rapoport, Cincinnati.

Diphosphoglyceric acid normally makes up about half of the organic acid-soluble phosphorus contained in the blood of human beings, rabbits and dogs. In vivo, under certain conditions its concentration in the blood cells has been found to change readily and within wide limits. It is an important nondiffusible anion in the blood cells, normally binding an amount of base about equal to that bound by hemoglobin. We have investigated the importance of this substance in the acid-base equilibrium of the blood cells in several conditions in which large changes of the diffusible blood electrolytes are known to occur. Three of these studies concerned (1) pyloric obstruction in a dog; (2) ammonium chloride acidosis in a human subject and (3) acidosis and dehydration due to diarrhea in a young infant. Changes in the concentration of organic acid-soluble phosphorus in the blood cells, which was previously found to be increased after pyloric obstruction and decreased with ammonium chloride acidosis, were due entirely to changes in the diphosphoglyceric acid fraction. In the acidotic infant, in whom the carbon dioxide content of the blood was 13 volumes per cent, the organic acid-soluble phosphorus content of the cells (normally 50 mg. per hundred cubic centimeters) was reduced to 23 mg. Treatment included the administration of a phosphate solution intravenously and by mouth, in addition to other fluids (solutions of sodium bicarbonate, dextrose and sodium chloride) given to combat the condition of acidosis and dehydration. During recovery, the organic acid-soluble phosphorus increased to its normal concentration in the blood cells within three days. Further studies along these lines are being carried on to determine how the administration of phosphate affects the changing electrolyte pattern of the blood in conditions of acidosis in which the organic acid-soluble phosphorus content is decreased and to ascertain the kind and amount of phosphate that can be used most advantageously in the treatment of such conditions.

Studies of Water Balance in Premature Infants: Correlation of Metabolic Measurements with Electrolyte Balance. Dr. H. H. Gordon and Dr. S. Z. Levine, New York.

The water and the electrolyte balance of 4 premature boys ranging in age from 17 to 31 days and in weight from 1,900 to 2,600 Gm. were studied in 9 observations of three to eleven days which totaled forty-eight days. The caloric,

the fluid and the protein intake were adequate to permit satisfactory daily gains in weight of 25 to 48 Gm.

The water balance was ascertained according to the principles of both the metabolic method of Newburgh and the electrolyte method of Gamble, Peters and Darrow. For the latter procedure, the chloride and the nitrogen balance were used as indexes of the extracellular and the intracellular water balance.

The close agreement in the results obtained by these two methods suggests that under carefully controlled environmental and dietary conditions either method of predicting the water balance of thriving premature infants is satisfactory.

In the presence of perceptible perspiration the electrolyte method is unsatisfactory, since the unmeasured excretion of electrolytes through the skin indicates values for retention which exceed the true values. Under such conditions the metabolic method yields better estimates of water balance, provided one makes a satisfactory determination of the total calories expended.

Evidence suggested that in carefully controlled studies on balance excretion of electrolytes through the skin may be responsible for the apparent discrepancy between the electrolyte and the water balance.

Possible Relation Between Electrolyte Balance and Bronchial Asthma. Dr. A. V. Stoesser and Dr. M. M. Cook, Minneapolis.

Several years ago one of us (A. V. S.) observed the advantageous effect of the ingestion of large amounts of dextrose in children with asthma. About the same time, McQuarrie, Thompson and Anderson called attention to the favorable influence of diets high in salt on the carbohydrate metabolism of diabetic children. The question then arose as to whether the ingestion of large amounts of sodium chloride would affect the benefits derived from the high carbohydrate diet in asthmatic children. The first few trials with a diet high in salt led in each instance to a definite increase in the asthmatic symptoms. Lowering the salt intake decreased the asthma, and this effect was enhanced by short periods of artificial fever or by the ingestion of potassium chloride.

These observations led to an investigation of the electrolyte metabolism in children with asthma. Patients who did not respond to the regular forms of therapy were chosen. The study was divided into various phases. Two asthmatic children were permitted to remain on a general diet with no restriction of salt. They were given artificial fever (with a temperature of 105 F.) for four hours, with no definite improvement. Four subjects received a diet low in salt but having adequate dietary constituents. The daily sodium chloride intake ranged from 120 to 200 mg. After ten days of this diet, with slight improvement in the asthma, artificial fever was given. One of the patients had a striking reduction in symptoms, and the remaining 3 had complete remissions. Two very young children with a less severe form of asthma repeatedly showed complete recession of symptoms with the low salt diet alone.

The 6 subjects on the low salt regimen, while in a period of remission, were given from 1 to 20 Gm. of sodium chloride per day. In all cases asthmatic symptoms reappeared, and in some instances the asthma was worse after the administration of the salt had been stopped. Four patients in whom remissions were not produced by the low salt diet with or without artificial fever received 6 to 10 Gm. of potassium chloride daily. The patients with less severe involvement gradually ceased to have asthmatic symptoms, while the others showed little change or aggravation. Prompt improvement, however, followed the discontinuance of the potassium chloride. Three children receiving the low salt diet during a state of remission were also given 6 to 10 Gm. of potassium chloride, and no asthma occurred during or after the administration of the salt.

The variations in the intake of the salts were associated in all patients with changes in weight and in hydration; this suggested the desirability of examining the relation between electrolyte and water balance in the mechanism of asthmatic attacks. McQuarrie and his co-workers have shown that pitressin causes not

only a retention of body water but a coincident increase in the output of sodium and chloride in the normal subject. Six asthmatic children who responded poorly to the low salt regime received pitressin and water as prescribed by McQuarrie. A total of 20 observations were made; in 18 there was a reduction in the number and severity of the attacks during and after the antidiuretic period. It appears that asthma may be aggravated by sodium chloride and mitigated by depletion of body salts, even in the presence of excessive hydration.

SIGNIFICANCE OF THE PNEUMOCOCCIC CARRIER STATE IN NEPHROTIC CHILDREN. DR. C. M. MACLEOD and DR. L. E. FARR, New York.

In nephrotic children pneumococcic peritonitis or bacteremia seems to be as much a part of the disease as are the deficit of plasma protein, albuminuria, lipemia, retention of salt and edema. In a group of nephrotic children isolated from other patients and removed as far as possible from outside contacts, we have been able to isolate the same strain of pneumococcus from the nasopharynx as that found in the peritoneal cavity or in the blood stream. Further, this carrier state may persist for a considerable time before peritonitis develops and after recovery from an attack.

Type-specific agglutinins do not uniformly develop after an attack, nor does their presence necessarily protect a patient or otherwise materially affect the outcome. When children in the nephrotic state are improving, the type of pneumococcus carried in the nasopharynx may change, or the pneumococci may entirely disappear. During the more severe nephrotic episodes the type carried tends to remain the same in any one patient.

DIET AND RESISTANCE TO INFECTION: FURTHER STUDIES. DR. C. F. CHURCH, MISS CLAIRE FOSTER and MISS DOROTHY W. ASHER, Philadelphia.

The factors influencing the resistance of the host to infection with Salmonella enteritidis have been subjected to further analysis. These factors involve the genetic and the dietary background and the external environment. By keeping all three constant, the survival curves of groups of 20 mice are reproducible within the limits of statistical variation. The virulence of the organism has remained unchanged for more than eighteen months.

Graphic analysis of the time survival data shows that the curve is biologically truncated (Bliss, C. I.: *Ann. Applied Biol.* **24**:815, 1937) at nine to twelve days. The deaths prior to this time conform to a normal frequency distribution, while subsequent deaths conform to a new frequency distribution with a diminished rate. This biphasic type of curve is explained by the antibody response of the surviving animals. The first part of the curve (prior to nine to twelve days) gives the true index to natural resistance. By plotting the results on probability paper one may ascertain the mean survival time for natural resistance uninfluenced by the development of immunity. This method of graphic analysis has been applied to data from dietary studies.

IMMUNOLOGIC RESPONSE TO INGESTION OF FOODS IN NORMAL AND ECZEMATOUS INFANTS. DR. V. W. LIPPARD, New York.

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

TREATMENT OF NEUROGENIC MEGACOLON WITH SELECTIVE DRUGS. DR. W. O. KLINGMAN, New York.

In the light of newer knowledge of the physiology and nerve control of the rectosigmoid region, a rational therapeutic approach to the problem of megacolon was attempted with properly selected drugs. A series of 7 cases was studied. Megacolon was demonstrated by barium sulfate enemas. It was apparent that cases of megacolon fall into two large groups: (1) a group (rectosigmoidal

achalasia) in which one finds a failure of the rectosigmoid apparatus to relax and (2) a group in which the rectosigmoid apparatus functions normally but there is failure of the motor function above the rectosigmoid region.

Among various drugs which were tried, two were found the selective action of which resulted in relief from the obstipation. In the cases of rectosigmoid achalasia in which the rectosigmoid apparatus failed to relax because of lack of proper inhibitory function of the parasympathetic system, syntropan, a drug atropine-like in action, was found to relieve the obstipation. In 5 cases of this type the disorder was successfully treated. In the case of motor weakness of the colon above the rectosigmoid apparatus in which the rectosigmoid apparatus functioned normally, prostigmine, a physostigmine-like drug, was used. In 1 case the condition was successfully treated. In the case of rectosigmoidal achalasia in which there was hyperactivity of the sympathetic system, no drug was found to be practical, and surgical treatment in the form of presacral resection was carried out, with relief from the obstipation.

On the basis of these clinical studies and of experience reported in the literature a classification of neurogenic megacolon is proposed:

1. Rectosigmoidal achalasia
   (*a*) Caused by motor hyperactivity of the sympathetic innervation to the rectosigmoidal apparatus
   (*b*) Caused by ineffective inhibitory function of the parasympathetic innervation to the recto-sigmoid apparatus
2. Deficient motor function of the innervation of the colon above the rectosigmoid apparatus.
   (*a*) Caused by deficient motor parasympathetic function
   (*b*) Caused by deficient sympathetic motor function

The work demonstrates an approach to the problem of megacolon on the basis of neurogenic unbalance. A classification of neurogenic disturbances resulting in megacolon with constipation was proposed on the basis of study with barium sulfate enemas and trial of appropriate drug therapy. Surgical treatment of neurogenic megacolon is advisable in these cases in which there is extreme overactivity of the sympathetic innervation to the rectosigmoidal apparatus. Selective drug therapy has proved effective when neurogenic unbalance exists because of faulty inhibitory or motor function of the parasympathetic system.

DECOLORIZATION OF METHYLTHIONINE CHLORIDE (METHYLENE BLUE) BY BLOOD OF INFANTS AND OLDER CHILDREN: CLINICAL APPLICATION AND MECHANISM OF THE REACTION. DR. C. H. SMITH, New York.

In the relation between the red cell and its environment, the occurrence of adsorptive phenomena is to be expected. The extensive surface provided by the cells, which are in intimate contact with the diverse of substances contained in plasma, suggests opportunities for adsorptive processes comparable to those which occur at other interfaces. Relatively few studies have been made in which this property of the red cells has been investigated.

In a previous study made with the blood of infants, a phenomenon was described in which dilute solutions of methylthionine chloride were decolorized by blood under well defined experimental conditions. The essential feature of this reaction was that the dye is removed from the solution by the red blood cells at ice box temperature. The removal of the dye by the cells, which permits visualization in dilute solutions, the peculiarities of temperature and the reversibility of the reaction conform to principles governing changes in surface tension associated with adsorption rather than with oxidation-reduction phenomena.

In the present study a series of tests for adsorption of dye were carried out by means of a simplified procedure which would apply to children of any age. The results of 576 tests revealed, in general, that with blood removed during the acute stage of disease adsorption of methylthionine chloride was at a minimum

(no decolorization), while with the blood of well children and of those recovering from disease moderate and at times marked decolorization occurred. The observations were correlated with the sedimentation rate of the blood, since the degree of decolorization of the dye appeared to be related to the speed with which erythrocytes settled out from mixtures of methylthionine chloride and blood. In several instances samples of blood were observed to sediment at parallel rates over a period of several hours, yet the degree of decolorization in these tubes was unequal; this suggested that the erythrocytes, in addition to being influenced by their own sedimentation rate, exhibit individual capacities for adsorbing dye. Unusual degrees of decolorization occurred with the blood of children with nutritional anemia who were receiving iron, even while the volume of packed cells was still below normal. The degree of adsorption in these cases compared with that noted previously for infants during the first four months of life.

The present study also revealed that a trace of serum or plasma (human being, horse or guinea pig) was essential in the adsorption of the dye by the erythrocytes.

While the experimental conditions by which decolorization of methylthionine chloride was demonstrated differ from those in circulating blood, the behavior of the red cell in this reaction suggests a basis for related physiologic phenomena. Studies have been recorded in which digestive products, toxins, drugs and various hormones are taken up in the body by the red cells. It may well be that adsorptive processes are partially responsible for their deposition on the red cell and for their subsequent transport through the blood stream. On the other hand, it remains to be determined whether the degree of adsorption of dye noted in these tests constitutes a measure of the adsorptive capacities of the red cell for unrelated substances.

Book Reviews

Leukemia and Allied Disorders. By Claude E. Forkner, M.D. Price, $5. Pp. 333, with 73 illustrations and 6 colored plates. New York: The Macmillan Company, 1938.

This informative monograph will be read with satisfaction both by clinicians and by hematologists. Dr. Forkner draws freely on his own experience, which is well founded in pathology as well as in clinical material, and he covers the hematologic literature with gratifying brevity and discrimination. He deals with the huge leukemic problem, presenting a thorough discussion of the fundamental aspects of the etiology, the pathologic physiology and the pathologic findings before taking up the detailed clinical picture and the hematologic features. An extensive bibliography is given.

Although no attempt to brief the material can be made here, to mention a few points of interest may stimulate the reader to look further.

The discussion of the etiologic factors emphasizes the truism that in spite of a literature replete with clinical and experimental observations the cause of leukemia remains an enigma. Evidence for and against the malignant versus the infectious nature of the disease is reviewed. Here observations on the experimental leukemia in mice and in fowl have proved of value. Whereas the experimental evidence seems to indicate a relation between malignant growth and leukemia, the nature of the agent is undetermined. That the transmission of lymphomatosis of mice, associated often with a leukemic blood picture, is dependent on the transmission of viable cells does not preclude the possibility that the agent is a filtrable virus, protected from destruction by the cell which is its host. The leukosis of fowl, transmissible by cell-free organ filtrates, supports the virus theory. However, the opinion that the filtrable virus is the causative agent of leukosis in fowls is not unchallenged.

As to the relation of infection to leukemia, numerous case studies are cited which illustrate the occurrence of an antecedent or concurrent infection. Dr. Forkner states that it is conceivable that "under the influence of an infectious agent, in individuals of a special physical or hereditary constitution, the origin of leukemia in some cases may be possible."

In the review of the physiologic aspects of the problem one is impressed with the paucity of relevant material to be gleaned from the many studies made during the past two decades. Confusion exists in the field of chemistry, possibly because of the variable nature of the disease. Positive facts are few, except as to nitrogen and phosphorus metabolism. Studies on cellular metabolism yield hardly more conclusive results, although there is some evidence that the oxygen consumption of cells (lymph nodes) in mice with spontaneous leukemia is greater than in normal animals and that this increased rate precedes any morphologic evidence of leukemia. It is known that leukemic cells contain proteolytic enzymes. This has been thought to be responsible for the growth-stimulating substance which has been observed in leukemic serums when they are added to normal cells. The behavior of leukemic leukocytes in tissue culture, while contributing to the morphologic study of these cells, has contributed little to the fundamental understanding of the disorder.

Dr. Forkner recognizes three types of leukemia: the myelogenous, the lymphatic and the monocytic form. It is to the last of these that he offers a more detailed personal contribution, describing a characteristic clinical, hematologic and pathologic picture which he believes identifies it as distinct from the myeloid type. He admits the difficulty of differentiation in certain cases of acute involvement, even with the help of histologic material, and relies on the structure of the lymph nodes, on cytologic changes and on the oxidase reactions of the tissues as diagnostic aids.

He devotes several chapters to the clinical and pathologic observations in cases of the acute and the chronic type in adults and one chapter to leukemia in children. Under the heading "allied conditions" he discusses chloroma, leukosarcoma, various rare types of cell and leukemoid states.

He discusses at length the revival of the arsenic treatment in the chloric forms of the disease, roentgen and radium therapy and, more briefly, other palliative procedures.

The monograph will be a valuable aid to the investigator and to the clinician alike.

Vaccinazione antitubercolare (vaccinazione coll' anatubercolina Petragnani). By Prof. Gaetano Salvioli. Price, 25 lire. Pp. 162, with 29 illustrations and 10 tables. Bologna: Licinio Cappelli, 1938.

This monograph is based on the work of Professor Salvioli with 100 children whom he vaccinated against tuberculosis with the anatuberculin of Petragnani. Most of the work was done on the children of the Foundling Hospital of Siena. He gives a large number of references to the literature. His six years' use of the vaccine prompted him to describe his experience so that it might be available to other physicians.

Professor Salvioli describes the vaccine as a preparation of tubercle bacilli killed with a 1 per cent solution of formaldehyde. The opalescent liquid containing the killed bacilli is used in the vaccination of the children. According to the author, the vaccine possesses all the antigenic characteristics of the live bacilli; it is capable of initiating an allergic state and of maintaining the vaccinal stimulus in the body for months.

The author notes a slowing up of the gain in weight in the first months after vaccination; however, the weight of the children reaches that of the nonvaccinated at the end of a year.

Professor Salvioli claims that a decreased mortality among the children of the foundling home was due to the fact that the children had been vaccinated with the anatuberculin. The average mortality before vaccination was 20.7 per cent and after it was 12 per cent. He seems to think that increased resistance to the various infective agents is produced among the vaccinated children.

The author used the vaccine orally and parenterally. However, he favors the intradermal method of administration. Premature, newborn and breast-fed infants were vaccinated with no evidence of primary toxicity.

One hundred vaccinated children were followed for from six months to five years, the majority for two to three years. Thirteen died, and on 10 of these autopsies were done. In only 1 case was tuberculosis given as the cause of death. Professor Salvioli believes this mortality to be extremely low compared with the death rate among those inoculated with BCG vaccine and those not vaccinated. During the period of observation 9 of the infants were accidentally exposed to a nurse with an open tuberculous lesion for approximately four weeks. Of these, 1 contracted a benign form of tuberculosis but at the end of five years enjoyed good health. The author uses this incident to show that vaccination with killed bacilli has a protective action of defense against tuberculosis.

The method of vaccination is perhaps better suited to the continent, where tuberculosis is more prevalent. It must also be pointed out that the vaccination frequently leaves a scar.

Tuberculosis Among Children and Young Adults. Second edition. By Dr. J. Arthur Myers. Price, $4.50, postpaid. Pp. 401, with 71 illustrations. Baltimore: Charles C. Thomas, 1938.

This book presents a thoroughly modern interpretation of the epidemiologic aspects of tuberculosis and makes a special plea for the cooperation of practicing physicians in the attempt to stamp out this infection. In view of what has been accomplished to date, this is not a utopian hope. Stress is laid on "first infection

types" (primary) as contrasted with "reinfection type" (secondary) of tuberculosis. The diagnosis and prognosis of each form are fully illustrated by roentgenograms. The outlined treatment is conservative. Special chapters are included: one on tuberculous meningitis and nontuberculous basal pulmonary disease by C. A. Stewart and one on tuberculous disease of the bones and joints by Paul W. Giessler. The chapter on recent progress of research on tuberculosis will be of great interest to many physicians. There is rather more repetition than usually is found, but possibly Dr. Myers intends by this means to emphasize his basic concepts on prevention. In his preface Allen K. Krause states that the book contains a "rich mine of information displayed as a whole for the first time."

News and Comment

UNIVERSITY NEWS

Medical College of the University of Virginia.—Dr. St. George T. Grinnan has been made emeritus professor of pediatrics, and Dr. Lee E. Sutton Jr. has been made professor of pediatrics.

CORRECTION

In the article by Doctors Langmann and Bruch entitled "Carcinoma of the Thyroid Gland in Children," in the September issue (**56**:616, 1938), the name "Lahey" at the end of the eleventh line under "Comment" on page 625 should read "Mayo," and the name "Mayo" in the middle of the fourteenth line in the same paragraph should read "Lahey."

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 9-12, 1940.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Kenneth Blackfan, 300 Longwood Ave., Boston.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

British Paediatric Association

President: Dr. Hector C. Cameron, 23 Devonshire Pl., Upper Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Sociedad Cubana de Pediatría

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: St. Louis. Time: May 15-19, 1939.

American Academy of Pediatrics

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Netherland Plaza Hotel, Cincinnati. Time: Nov. 16-18, 1939.
Region I. Place: Hotel Seneca, Rochester, N. Y. Time: Nov. 11-12, 1938.
Region II. Place: Skirven Hotel, Oklahoma City. Time: Nov. 16, 1938.
Region III. Place: Statler Hotel, Detroit, Mich., and Ann Arbor, Mich. Time: Oct. 27-29, 1938.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Skytop Lodge, Skytop, Pa. Time: April 27-29, 1939.

Canadian Society for the Study of Diseases of Children

President: Dr. R. R. MacGregor, 142 Wellington St., Kingston, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Charles E. Conrad, 209-210 Professional Bldg., Harrisburg, Va.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Place: Oklahoma City. Time: Nov. 15-18, 1938.

STATE

Alabama Pediatric Society

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.
Place: Montgomery. Time: April 17, 1939.

Arkansas State Pediatric Association

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Hot Springs. Time: January 1939.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

Florida State Pediatric Society

President: Dr. Gilbert S. Osincup, 300 E. Colonial Dr., Orlando.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Charles Hall Farmer, 553 Walnut St., Macon.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Scientific Meeting—Place: Augusta. Time: December 1938.
Business Meeting—Place: Atlanta. Time: April 1939.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. C. V. Calvin, 144 Golden Hill St., Bridgeport.
Secretary: Dr. E. T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

Indiana State Pediatric Society

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Secretary-Treasurer: Dr. Philip C. de Verges, 312 Audubon Bldg., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John P. Scott, 1740 Bainbridge St., Philadelphia.
Secretary: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. W. Myers Hunter, 306 N. Tryon St., Charlotte.
Secretary: Dr. J. R. Adams, 412 N. Church St., Charlotte.

Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. Mylnor W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

Tennessee State Pediatric Society

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Jackson. Time: April 11, 1939.

Texas Pediatric Society

President: Dr. F. O. Calaway, 3306 Fannin St., Houston.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Houston. Time: May 9, 1939.

Virginia Pediatric Society

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.
Place: Danville, Va. Time: October 1938.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Secretary: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Joseph K. Calvin, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. W. H. Bradford, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140 Second Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St., N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. John K. Glen, 4412 Montrose Blvd., Houston, Texas.
Secretary-Treasurer: Dr. J. L. Collier, 1620 Medical Arts Bldg., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Urban Busiek, 200 E. Pershing St., Springfield, Mo.
Secretary: Dr. Fred Speer, 2700 Parallel Ave., Kansas City, Kan.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sidney D. Kramer, 61 Eastern Parkway, Brooklyn.
Secretary: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Joseph Shimpa, 2309 N. 36th St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Hyman Green, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Julian M. Lyon, 40 Llanfair Rd., Ardmore, Pa.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to June, inclusive.

Richmond Pediatric Society

President: Dr. A. S. Hurt, 1028 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month, except July, August and September.

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Walter B. Seelye, 1305–4th Ave., Seattle.
Secretary: Dr. Armin Rembe, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Damon O. Walthall, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Horace H. Rackham Graduate School, Ann Arbor, Mich. Time: Nov. 11-12, 1938.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.